A STUDY ON CLINICAL PROFILE OF HASHIMOTO'S THYROIDITIS PATIENTS AT GOVT. STANLEY HOSPITAL

Dissertation
Submitted in partial fulfilment of the regulation of

M.D. DEGREE EXAMINATION

BRANCH I GENERAL MEDICINE

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GOVT. STANLEY MEDICAL COLLEGE AND HOSPITAL
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THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY
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CERTIFICATE

This is to certify that this dissertation titled

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I, **Dr. SUBBURAJ. D.,** solemnly declare that the dissertation titled **"A STUDY ON CLINICAL PROFILE OF HASHIMOTO'S THYROIDITIS PATIENTS AT GOVT. STANLEY HOSPITAL"** Is a bonafide work done by me at Govt. Stanley Medical College and Hospital from January 2012 to November 2012 under the guidance and supervision of my unit chief,

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DR. SUBBURAJ D

LIST OF ABBREVIATION

1. OP. NO. - Out patient number
2. IP No. - In patient number
3. MNG - Multinodular goiter
4. Diffuse- Diffuse goiter
5. SNT - Solitary nodule thyroid
6. TSH - Thyroid stimulating hormone
7. Hypo - Hypothyroidism
8. Hyper- Hyperthyroidism
9. HPR - Histopathological report
10. TPO –Thyroid peroxidase
11. TGb–thyro globulin
12. Neo - Neomercazole
13. Prop- Propranolol
14. FNAC- fine needle aspiration cytology
15. D- DEIODINASE
16. FLT – Focal Lymphocytic thyroidits
17. JAT- Juvenile autoimmune thyroidits

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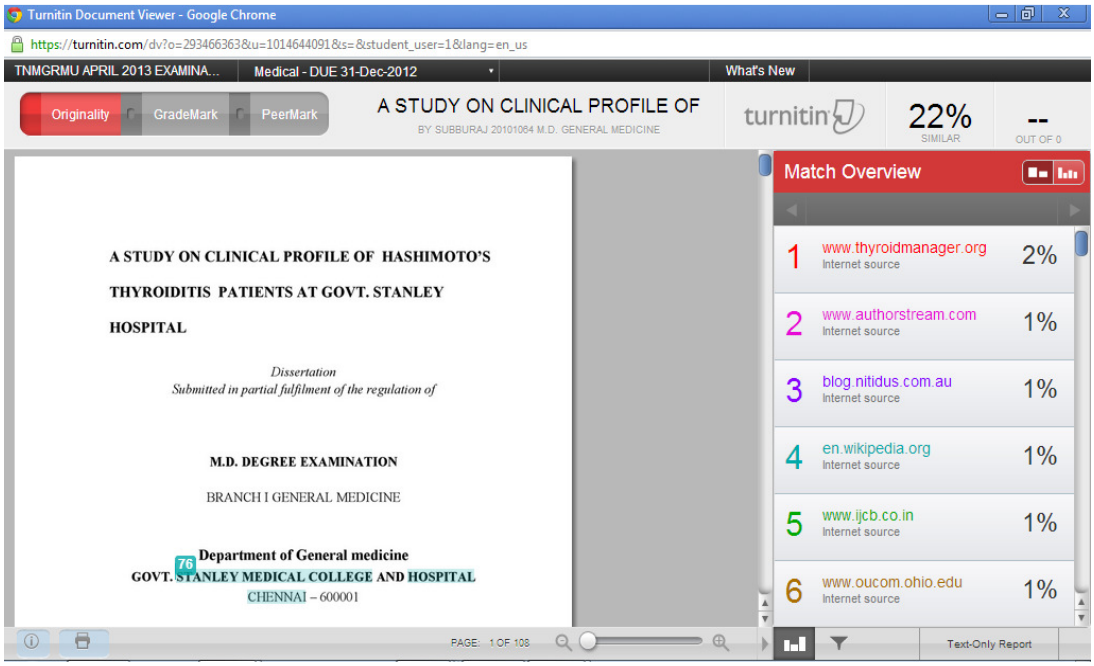
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INTRODUCTION

Hashimoto's thyroiditis, a well known condition affecting the thyroid gland is often under diagnosed due to its wide spectrum of clinical manifestations. As such it could present as a multinodular goitre, a diffuse goitre or a solitary nodule with features of hypothyroidism, hyperthyroidism or in a euthyroid state. It is the commonest cause of goitre with hypothyroidism in iodine sufficient areas. Since Hakaru Hashimoto discovered chronic lymphocytic infiltration in the thyroid in 1912, a sea change has occurred in our knowledge of this autoimmune process. It is now well documented that not all cases with histological features of lymphocytic infiltration are due to Hashimoto's thyroiditis. This histological picture of lymphocytic infiltration is also seen in some other conditions affecting the thyroid. The bio-chemical evaluation of autoantibody titres (AMA, ATG) together with the clinical, FNAC and hormone assay guides the clinician towards making a diagnosis of Hashimoto's thyroiditis. This condition is managed conservatively and surgery is rarely required.

REVIEW OF LITERATURE

HISTORICAL REVIEW

Hashimoto's thyroiditis, named after Japanese physician Dr. Haraku hashimoto. He was born in 1881, to a family of medical practitioners in midau, Japan. At the age of twenty two, he entered tomedical schoolat Kyushu university. He was graduated in 1907.[1]

In 1912, Hashimoto noticed lymphocytic infiltration in post operative thyroid gland biopsy, he named that disorder as struma lymphomatosa. He described struma lymphomatosa in his M.D thesis which was published in a german medical journal. He described important biopsy findings in his article, like diffuse lymphocytic infiltration, fibrosis, parenchymal atrophy.[2] The same clinical and biopsy findings were described by many physicians subsequently in both adult and paediatric age groups. This disorder is known as Hashimoto's thyroiditis or auto immune thyroiditis. Some authors named as chronic thyroiditis, lymphocytic thyroiditis, lymphadenoid goiter. His report explained why hypothyroidism is common even in developed countries, where iodine deficiency is rare.

Fig 1.Dr. Hakaru Hashimoto (1881-1934)

Fig 2Explanation board in kyushi university in japan about Dr Hashimoto

The disease usually manifest as painless, diffuse thyroid swelling in a young or middle-aged woman. It is frequently associated with hypothyroidism. The disease was thought to be rare, and the diagnosis was usually made by the operating surgeon at the time of surgery or by the pathologist after thyroidectomy. FNAC and serologic tests for thyroid auto antibodies have made the diagnosis very easy. It is the reason to believe that it may be increasing in frequency.[(2)] It is now one of the most common thyroid disorders and it is the most common cause of hypothyroidism.

Fromm et al described the elevation of the plasma gamma globulin fraction in hashimoto's thyroiditis patients[(4)]. He also described abnormal serum flocculation test[(4)]. These findings indicated that the disease might be related to a long-continued autoimmune reaction.

Rose and Witebsky[5] immunized the rabbits with extracts of rabbit thyroids and they removed the thyroid glands of the rabbits. They noticed the histological changes in the thyroid glands similar to Hashimoto's thyroiditis. They also found antithyroglobulin antibodies in the blood of the animals.

In 1956, Roitt et al.[6] noticed that a precipitate formed when an extract of human thyroid gland was added to serum from a patient with Hashimoto's thyroiditis. These antibodies might be responsible for the disease process. These original observations led directly to entirely new concepts of the causation of disease by autoimmunization.

The debate about the association between Hashimoto's thyroiditis and Graves' disease has been ongoing for many decades as they differ in clinical and immunological presentation. However, Hashimoto's thyroiditis and Graves' disease, which depict the two extremes of the clinical spectrum, are now included in a common entity called autoimmune thyroid disease. It is now believed that they share a common autoimmune pathology and are believed to be triggered by multiple genetic and environmental factors.

THYROID PHYSIOLOGY

Thyroid produces triiodothyronine (T_3), thyroxine (T_4), and calcitonin. Up to 80% of the T_4 is converted to T_3 by peripheral organs such as the liver ,spleen & kidney. T_3 is more powerful than T_4, which is largely a prohormone, perhaps four or even ten times more active.

Iodine Metabolism

Iodine ingested as drinking water, sea fish, salt, milk and eggs is converted toiodide and absorbed in the small intestine. 98% of the absorbed iodide is taken up by the thyroid gland and the remaining is excreted by the kidneys. The thyroid takes up about 50 to 100 micro grams and the kidney eliminates around 150 to 500 mg through urine. Iodide clearance is dependent on the glomerular filtration rate (GFR) and increases and decreases with enhancement or reduction of GFR.[8]

Thyroid hormone synthesis

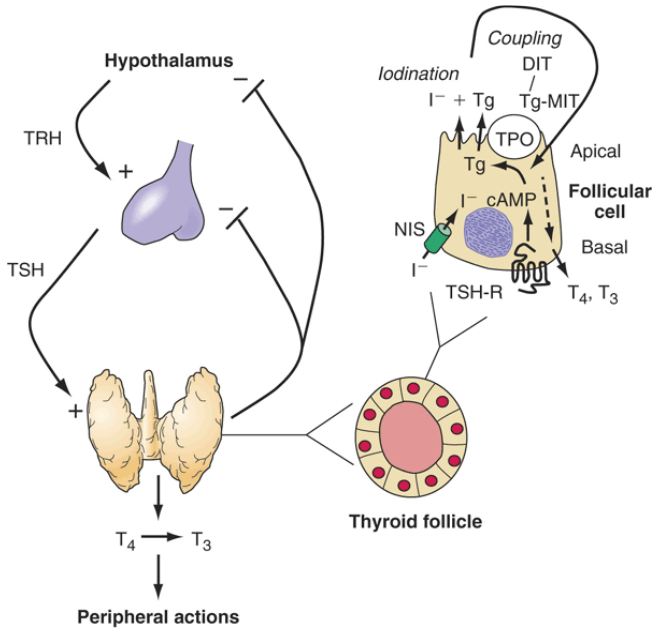


Fig 3: Thyroid hormone synthesis & regulation

Thyroxine (T_4) is produced in follicular cells from free tyrosine and on the tyrosine residues of the thyroglobulin (Tg). Tgb is synthesized in the rough endoplasmic reticulam and enter the colloid in the lumen. Meanwhile, a Na/I symporter pumps iodide (I^-) actively into the cell. The thyroid concentrates iodide actively transporting it from the circulation to the colloid. The transport mechanism is called "the iodide trapping mechanism". In the thyroid gland iodide is oxidized to iodine by the enzyme peroxidase. This iodine in a matter of seconds is attached to the 3 position of the tyrosine molecule to form monoiodotyrosine. Monoiodotyrosine is next iodinated in the 5-position to form

diiodotyrosine. Two diiodotyrosine molecules then undergo oxidative condensation to fom thyroxine. One molecule of DIT combines with one molecule of MIT to form triiodothyronine(T3).[9]

Upon stimulation by the TSH, thyroglobulin taken up by follicular cells. It cleaves the iodinated tyrosines from Tg in lysosomes, forming T_4 and T_3, and releasing them into the blood. Deiodinese enzymes convert T_4 to T_3 .Thyroid hormone secreted from the gland is about 80-90% is T_4 & about 10-20% is T_3.

Regulation of Thyroid Activity

Thyrotropin releasing hormone (TRH) is produced by the hypothalamus and stimulates anterior pituitary cells to secrete Thyroid stimulating hormone (TSH), which in turn stimulates all processes leading to synthesis of thyroid hormone. TSH stimulates thyroid function, increasing iodine uptake and thyroxine synthesis, increasing blood flow, causing cell hypertrophy and increasing the weight of the gland. TSH acts by increasing cyclic AMP formation. Thyroxine in turn inhibits TSH secretion which is known as "negative feedback mechanism"[9]. The negative feedback control between thyroid hormone production and the stimulating hormones has long been known. TSH from the anterior pituitary has s stimulating effect on T3/T4 Production. TRH which is

stored in the hypothalamus, is a stimulator of TSH Production. TRH reaches the anterior pituitary via the pituitary venous portal system. Therefore, with increased TRH stimulation, TSH production is raised with a consequent rise in T3/T4 output from the thyroid. Rising levels of T3/T4 (Primarily a rising T3 concentration) have an inhibitory effect on the TRH/TSH axis. Thus there is an elegant mechanism in place for the precise control of the production and release of thyroid hormones. In reality the secretion of thyroid hormones is under a far greater range of control than this simple feedback arrangement. The gland itself can auto regulate according to the supply of iodine (increasing concentrations of iodine are inhibitory) and the thyroid gland itself can produce antibodies which may either stimulatory or inhibitory to thyroid function.[11]

Mechanism of Thyroid Hormone Action

Thyroid hormone binds to a specific nuclear thyroid hormone receptor (TR), which in turn, binds to DNA , usually as a heterodimer with retinoid X receptor at specific sequences (thyroid hormone response elements, or tres) dictated by the DNA binding-site preferences of the RXR-TR (or TR-TR) complex . Triiodothyronine has a 15-fold higher binding affinity for trs than does T_4, explaining its function as the active thyroid hormone. In humans, there are two TR genes, α and β, found on

different chromosomes (trα, chromosome 17; trβ, chromosome 3). There are several alternatively spliced gene products from each of these genes forming both active and inactive gene products. The active proteins are $tr\alpha_1$, and trs β_1, β_2, and β_3.[11] The structure of the trs conforms to a protein with three major functional domains, one binding DNA, one binding ligand, and a major transcriptional activation domain in the carboxy-terminus.

T3 is the active hormone and has many sites of action within the cell. The main effects are seen on the cell membrane, on the mitochondria and the cell nucleus. At the cell membrane level there is increased uptake of amino acids and glucose via the NA+/ K+ ATPase pump when T3 stimulation occurs. The effect on mitochondria is to increase energy production. T3 combines with T3 receptors within the nucleus. These cause a change of activity, either increased or decreased on mrna, with consequent effects on protein synthesis.(11)

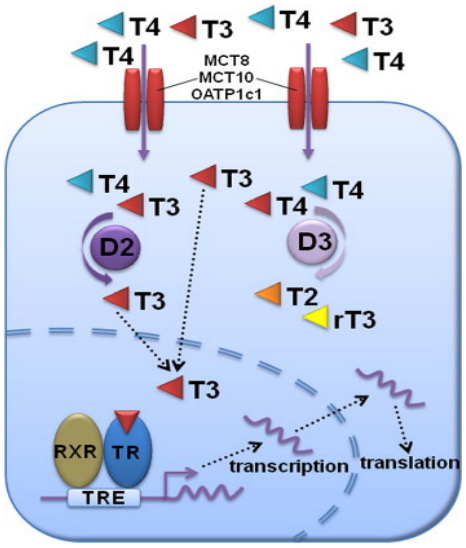


Fig 4: Schematic diagram of thyroid hormone activation and inactivation in a cell expressing D2 and D3. The T_3 that enters the cell can either be deiodinated to 3,3′-T_2 or enter the nucleus and bind to the thyroid hormone receptor. An additional source of T_3 is that generated by outer ring deiodination of T_4 within the cell. The interaction of T_3 with the thyroid hormone receptor (TR) bound as a heterodimer with retinoid X receptor (RXR) to the thyroid hormone–response element (TRE), usually in the 5′ flanking region of a T_3-responsive gene, causes either an increase or a decrease in the transcription of that gene. This leads to parallel changes in the concentrations of critical proteins, thus producing the thyroid hormone response characteristic of a given cell.

Effects of Thyroid Hormoneon Specific Bodily Mechanisms

Stimulation of Carbohydrate Metabolism.

Thyroid hormone stimulates carbohydrate metabolism, including rapid uptake of glucose by the cells, enhanced glycolysis, enhanced gluconeogenesis, increased rate of absorption from the gastrointestinal tract, and increased insulin secretion with its resultant secondary effects on carbohydrate metabolism. All these effects probably result from the over all increase in cellular metabolic enzymes caused by thyroid hormone. Though utilization of sugar by the tissues is increased, glycogenolysis and gluconeogenesis in liver as well as faster absorption of glucose from intestines more than compensate it.

Stimulation of Fat Metabolism.

T4 and T3 indirectly enchance lipolysis by potentiating the action of catecholamines and other lipolytic hormones, probably by suppressing a phosphodiesterase leads to increased cAmp: plasma free fatty acids levels are elevated. Lipogenesis is also stimulated. All phase of cholesterol metabolism are accelerated, but its conversion to bile acids dominates. Thyroid hormone decreases the fat stores of the body to a greater extent than almost any other tissue element.

Effect on Plasma and Liver Fats.

Increased thyroid hormone *decreases* the concentrations of cholesterol, phospholipids, and triglycerides in the plasma, even though it *increases* the free fatty acids. Conversely, *decreased* thyroid secretion greatly *increases* the plasma concentrations of cholesterol, phospholipids, and triglycerides and almost always causes excessive deposition of fat in the liver as well. The large increase in circulating plasma cholesterol in prolonged hypothyroidism is often associated with severe atherosclerosis. One of the mechanisms by which thyroid hormone decreases the plasma cholesterol concentration is to increase significantly the rate of cholesterol secretion.

In the bile and consequent loss in the feces. A possible mechanism for the increased cholesterol secretion is that thyroid hormone induces increased numbers of low-density lipoprotein receptors on the liver cells, leading to rapid removal of low-density lipoproteins from the plasma by the liver and subsequent secretion of cholesterol in these lipoproteins by the liver cells.

Increased Requirement for Vitamins.

Thyroid hormone increases the quantities of many bodily enzymes and because vitamins are essential parts of some of the enzymes or coenzymes, thyroid hormone causes increased need for vitamins. Therefore, a relative vitamin deficiency can occur when excess thyroid hormone is secreted, unless at the same time increased quantities of vitamins are made available.

Increased Basal Metabolic Rate

Because thyroid hormone increases metabolism in almost all cells of the body, excessive quantities of the hormone can occasionally increase the basal metabolic rate 60 to100 per cent above normal. Conversely, when no thyroid hormone is produced, the basal metabolic rate falls almost to one-half normal. Extreme amounts of the hormones are required to cause very high basal metabolic rate. Thyroid hormone is important for maintaining body temperature. However, metabolic rate in spleen, brain, gonads, uterus, and lymph nodes is not significantly affected. The mechanism of calorigenesis was believed to be uncoupling of oxidative phosphorilation: excess energy being released as heat. However, this occurs only at very high doses of and is not involved in mediating the physiological actions of T3, T4.[14]

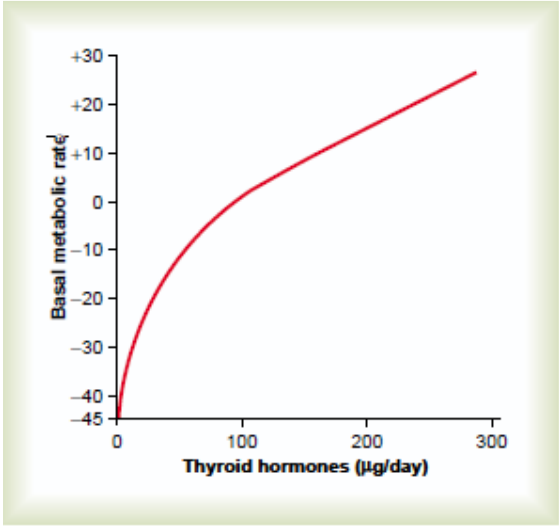


Fig 5: Relationship between BMR & thyroid hormones

Decreased Body Weight

Thyroid hormone almost always has inverse relationship with body weight. Increased thyroid hormone always decreases the body weight, and decreased hormone always increases the body weight. These effects do not always occur, why because, thyroid hormone also increases the appetite and this may counterbalance the change in the metabolic rate.

Effect of Thyroid Hormones on the Cardiovascular System

Increased Blood Flow and Cardiac Output

Metabolism in the tissues increased which results in increased utilization of oxygen more than normal. The metabolic end products from the tissues release of greater than normal quantities. These effects cause

vasodilatation in most body tissues, thus increasing blood flow. The rate of blood flow in the skin especially increases because of the increased need for heat elimination from the body. As a consequence of the increased blood flow, cardiac output increases, sometimes rising to 60 per cent or more above normal when excessive thyroid hormone is present and falling to only 50 per cent of normal in very severe hypothyroidism.[15]

Increased Heart Rate

The heart rate increases considerably more under the influence of thyroid hormone than would be expected from the increase in cardiac output. Therefore, thyroid hormone seems to have a direct effect on the excitability of the heart, which in turn increases the heart rate. This effect is of particular importance because the heart rate is one of the sensitive physical signs that the clinician uses indetermining whether a patient has excessive or diminished thyroid hormone production. It also modifies cardiac specific genes to improve cardiac contraction.[15]

Increased Heart Strength

The heart rate increases considerably more under the influence of thyroid hormone than would be expected from the increase in cardiac output. Therefore, thyroid hormone seems to have a direct effect on the

excitability of the heart, which in turn increases the heart rate. This effect is of particular importance because the heart rate is one of the sensitive physical signs that the clinician uses indetermining whether a patient has excessive or diminished thyroid hormone production.

The increased enzymatic activity caused by increased thyroid hormone production apparently increases the strength of the heart when only a slight excess of thyroid hormone is secreted. This is analogous to the increase in heart strength that occurs in mild fevers and during exercise. However, when thyroid hormone is increased markedly, the heart muscle strength becomes depressed because of long-term excessive protein catabolism. Indeed, some severely thyrotoxic patients die of cardiac decompensation secondary to myocardial failure and to increased cardiac load imposed by the increase in cardiac output.

Normal Arterial Pressure

The *mean* arterial pressure usually remains about normal after administration of thyroid hormone. Because of increased blood flow through the tissues between heartbeats, the pulse pressure is often increased, with the systolic pressure elevated in hyperthyroidism to 10 to 15 mm Hg and the diastolic pressure reduced a to corresponding amount.

Increased Respiration

The increased rate of metabolism increases the utilization of oxygen and formation of carbon dioxide; these effects activate all the mechanisms that increase the rate and depth of respiration.

Increased Gastrointestinal Motility

It also increases appetite and food intake, thyroid hormone increases both the rate of secretion of the digestive juices and the motility of the gastrointestinal tract. Hyperthyroidism often results in diarrhea. Lack of thyroid hormone can cause constipation.

Excitatory Effects on the Central Nervous System

In general, thyroid hormone increases the rapidity of cerebration but also often dissociates this; conversely, lack of thyroid hormone decreases this function. The hyperthyroid individual is likely to have extreme nervousness and many psychoneurotic tendencies, such as anxiety complexes, extreme worry, and paranoia.[18]

Effect on the Function of the Muscles

Slight increase in thyroid hormone usually makes the muscles react with rigor, but when the quantity of hormone becomes excessive, the muscles become weakened because of excess protein catabolism. Conversely, lack of thyroid hormone causes the muscles to become sluggish, and they relax slowly after a contraction.

Muscle Tremor

One of the most characteristic signs of hyperthyroidism is a fine muscle tremor. This is not the coarse tremor that occurs in Parkinson's disease or in shivering, because it occurs at the rapid frequency of 10 to 15 times per second. The tremor can be observed easily by placing a sheet of paper on the extended fingers and noting the degree of vibration of the paper. This tremor is believed to be caused by increased reactivity of the neuronal synapses in the areas of the spinal cord that control muscle tone. The tremor is an important means for assessing the degree of thyroid hormone effect on the central nervous system.[18]

Effect on Sleep

Because of the exhausting effect of thyroid hormone on the musculature and on the central nervous system, the hyperthyroid subject often has a feeling of constant tiredness, but because of the excitable effects of thyroid hormone on the synapses, it is difficult to sleep. Conversely, extreme somnolence is characteristic of hypothyroidism, with sleep sometimes blasting 12 to 14 hours a day.[18]

Effect on Other Endocrine Glands

Increased thyroid hormone increases the rates of secretion of most other endocrine glands, but it also increases the need of the tissues for the hormones. For instance, increased thyroxine secretion increases the rate of glucose metabolism everywhere in the body and therefore causes a corresponding need for increased insulin secretion by the pancreas. Also, thyroid hormone increases many metabolic activities related to bone formation and, as a consequence, increases the need for parathyroid hormone. Thyroid hormone also increases the rate at which adrenal glucocorticoids are inactivated by the liver. This leads to feedback increase in adrenocorticotropic hormone production by the anterior pituitary and, therefore, increased rate of glucocorticoid secretion by the adrenal glands.

Effect of Thyroid Hormone on Sexual Function

For normal sexual function, thyroid secretion needs to be appropriately normal.

In men, lack of thyroid hormone is likely to cause loss of libido; great excesses of the hormone, however, sometimes cause impotence. In women, lack of thyroid hormone often causes *menorrhagia* and *polymenorrhea*— that is, respectively, excessive and frequent menstrual bleeding. Yet, strangely enough, in other women thyroid lack may cause irregular periods and occasionally even *amenorrhea*. A hypothyroid woman, like a man, is likely to have greatly decreased libido. To make the picture still more confusing, in the hyperthyroid woman, *oligomenorrhea*, which means greatly reduced bleeding, is common, and occasionally amenorrhea results. The action of thyroid hormone on the gonads cannot be pinpointed to a specific function but probably results from a combination of direct metabolic effects on the gonads as well as excitatory and inhibitory feedback effects operating through the anterior pituitary hormones that control the sexual functions.

THYROIDITIS

Thyroiditis is a term indicating the presence of thyroid inflammation, and thus comprises a large group of diverse inflammatory conditions.[19]

Not only the causes of thyroiditis are extremely varied, their clinical presentations may also be diverse and are difficult to categorize in a simple fashion. Thus, autoimmune thyroiditis may present with hypothyroidism but often patients remain euthyroid for long periods after the disease is initiated. On the other hand, in a euthyroid patient with Hashimoto's disease who becomes pregnant, the postpartum period is often complicated by an acute form of hyperthyroidism due to the transient exacerbation of thyroiditis, often followed by a period of hypothyroidism .[19]

Classification of Thyroiditis [19]

- Acute thyroiditis
- Subacute thyrioditis
    - Subacute Granulomatous Thyrioditis
    - Subacute Lymphocytic Thyrioditis

- Chronic Thyroiditis
    - Chronic Lymphocytic Thyroiditis (Hashimoto's)
    - Invasive fibrous Thyroidits (Reidel's)

CAUSES OF THYROIDITIS

Autoimmune thyroiditis
Postpartum, silent, or painless thyroiditis
Subacute (nonsuppurative) thyroiditis
Acute infectious thyroiditis
Riedel's thyroiditis
Postirradiation (^{131}I or external-beam therapy)
Sarcoidosis

Acute Thyroiditis[19]

Acute thyroiditis (Acute suppurative thyroiditis, pyogenic thyroiditis, bacterial thyroiditis) is an uncommon inflammatory disease, usually bacterial in origin; it can be caused by fungi, other parasitic organisms or even pnemocystis carinii. The most common bacterial agents are streptococcus pyogenes, staphylococcous aureus and

pneumococcous pneumoniae. Other bacteria like E.Colli, H .influenza and meningococcal organisms as well as anaerobes have been reported to cause infection. Acute thyroiditis was much more common in the pre antibiotic era.[27] The clinical picture is that of thyroid "cellulitis" or "abscess" and the diagnosis may be established by needle aspiration and micro serological studies.

Treatment is rest, local heat and antibiotics. Occasionally an abscess develops, which requires open surgical drainage or thyroid lobectomy.

Subacute Thyroiditis

Subacute thyroiditis may be subdivided into subacute granulamatous thyroiditis, which is characteristically painful, and subacute Lymphocytic thyroiditis, which is painless. Both these disorders, although distinct histologically and most likely etiologically, are strikingly similar in terms of clinical thyroid dysfunction and duration, and hence are included within the same general classification. [19]

Subacute Granulamatous (painful) Thyroiditis

In 1904, de Quervain described granulamatous changes and giant cells in thyroid glands of patients presented with painful thyroid swelling. It is the commonest cause of a painful thryroid. Subacute Granulamatous thyroiditis is almost always most viral in origin, being closely associated with outbreaks of mumps, and also other viruses like adeno, Coxsackie, influenza and infectious mononucleosis. It tends to show a seasonal variation (Summer and fall) and is associated with a viral prodrome. Susceptibility appears to be genetically determined.

Most common symptom is painful swelling, which is often perceived as a "sore throat", or pain in the ears. The thyroid gland is usually enlarged often asymmetrically and is tender and firm. The average duration is two to five months. Initially in the first few weeks about half the patients have signs and symptoms of hyperthyroidism, which is due to destruction of thyroid parenchyma with subsequent release of preformed hormone. Hyperthyroidism persists for two to six weeks and is followed by euthyroid state, which sometimes progresses to transient hypothyroidism. The ESR is nearly always elevated usually>50 mm/hr. A normal ESR virtually excludes the diagnosis of activedisease.[19] The WBC count is normal or slightly elevated.[19] FNAC is useful for

confirmation but not always needed. Radioactive iodine uptake is extremely low. In most cases pain is controlled with aspirin and only rarely steroid is indicated. If the associated hyperthyroidism requires a symptomatic treatment, betaadrenergic blockade with propranol is usually sufficient. Antithyroid drugs are not indicated, as the hyperthyroid state is due to the release of preformed hormones from destruction of the gland, and not due to an increase in thyroid hormone synthesis. Subacute granulamatous thyroiditis is self-limiting and almost always goes onto complete recovery.[19]

Subacute Lymphocytic (painless) Thyroiditis

This is an entity characterized by hypothyroidism, a suppressed radioactive iodine uptake and painless goiter. In about 50% of the cases, a palpable thyroid swelling is not present and hence the term silent thyroiditis has also been used.[27] Painless thyroiditis exists in two forms, either occurring sporadically or in the postpartum periods.[27]

Current evidence suggest an autoimmune basis for painless thyroiditis with approximately 50% of the patient with sporadic type having thyroid microsomal antibodies and histological evidence of lymphocytic infiltration. There is complete resolution of the histological changes following recovery.[19]

Postpartum painless thyroiditis is almost certainly autoimmune in origin occurring in successive pregnancies and associated with other autoimmune thyroid diseases.[19] Painless thyroiditis is characterized a relatively abrupt onset of the symptoms of hyperthyroidism, with a small, firm, non-tender goitre. As mentioned before goitre may be absent in about 50% of the cases. However, patients with postpartum painless thyroiditis could present with symptoms and biochemical features of hyper or hypothyroidism.[19]

Treatment of this condition is often limited to reassurance and observation. During the hyperthyroid phase in most patients, the signs and symptoms can be managed effectively with beta adrenergic blockade. Steroids appear to be of little value and are not indicated. [19] When postpartum painless thyroiditis presents with hypothyroidism, thyroxine replacement therapy is indicated.[19]

Invasive Fibrous Thyroiditis (Riedel's Thyroiditis)

In 1896, Riedel first described rarest form of thyroiditis[19] Riedel's thyroiditis is a rare disease of unknown origin, predominantly affecting middle aged women between 30 and 60, in whom the thyroid parenchyma is replaced by dense fibrous tissue. The patient usually present with a history of long standing, painless anterior neck enlargement, that

progresses gradually to produce pressure symptoms like dysphagia, and occasionally even respiratory obstruction.[19] The gland is typically stony hard and often requires wedge biopsy or lobectomy to exclude malignancy. This condition is characterized by fibrosis of the thyroid gland and adjacent structures and may be associated with fibrosis elsewhere, especially in the retroperitoneal area.

Resection of the isthmus or other areas of involved thyroid tissue may often relieve symptoms. Complete surgical resection generally should not be attempted because the fibrotic process obliterates the tissue planes thereby making the procedure difficult and probably hazardous. Most of the patients are euthyroid, and thyroid hormone replacement therapy is indicated only in cases of hypothyroidism.[19] Hypothyroidism develops as a consequence of all viable thyroid tissue being replaced by the fibrotic process.[19]

The disease has been known to stabilize or spontaneously regress, and curiously despite the invasive nature of the disease process, recurrences after resection are rare, and the prognosis is generally favorable.[19,20]

HASHIMOTO'S THYROIDITIS

INTRODUCTION

Hashimoto's thyroiditis is a most common autoimmune disorder, which causes significant morbidity. Its pathophysiological hallmark is lymphocytic infiltration of thyroid follicles resulting in autoimmune glandular destruction. Various studies have successfully outlined the genetic and environmental factors responsible for the causation of the disease. Hashimoto's thyroiditis serves as a paradigm not just for disease of the thyroid gland, but also for autoimmune disease in the human body.

EPIDEMIOLOGY

The incidence of autoimmune thyroiditis has increased dramatically over the past few decades, affecting up to 5% of the general population in iodine sufficient areas. The prevalence reported in the studies varies mainly depending on the diagnostic criteria, ethnicity, iodine status and age or sex of the population studied.[21,22] Autoimmune thyroiditis is being increasingly identified in the young population due to various reasons, such as increasing awareness, availability of better antibody assays, and skilled cytopathologists to perform and interpret fine needle aspirations. The disease is 15 – 20 times as frequent in women as

in men.[21,22,23] It occurs especially during the decades from 30 to 50, but may be seen in any age group, including children, rare below 3 years. Determining the exact incidence and prevalence rates for Hashimoto's thyroiditis has been difficult due to variable expression of this disease increasing. Family studies always bring to light a number of relatives with moderate enlargement of the thyroid gland suggestive of Hashimoto's thyroiditis. Many of these persons have TG and TPO antibodies, and most are entirely asymptomatic.[24]

In 2010, Staii et al[29] conducted a study which showed current prevalence rate in the United States ranges between 0.3%-1.2%. Other studies (Wang et al., 1997) estimate the prevalence among the general population to be approximately 2%. When ultrasound guided biopsy was used to characterize the prevalence prospectively, with the aid of organized programs, the prevalence described has been at least 5% among the general population. It should be noted that studies employing the diagnostic modality of ultrasound guided biopsy have recorded prevalence rates higher than studies using other investigative modalities (Staii et al., 2010).[29]

The National Health and Nutrition Evaluation Study-3 (NHANES-3) studies has shown the prevalence of subclinical and clinical hypothyroidism to be 4.6% and 0.3%, respectively, in the United States (Hollowell et al., 2002)[39]. The Whickham survey, an epidemiological study conducted in the United States, has revealed the prevalence of hypothyroidism to be 1.5% in females and less than 0.1% in males (Tunbridge et al., 1997)[40].

During the past few decades there has been a reported increase in the incidence of Hashimoto's thyroiditis, which could be attributed to newer diagnostic modalities such as needle biopsies and serological tests, and their increased sensitivity when compared to the older methods. (mcconahey et al., 1962)[41]. Studies about age-specific incidence rates of Hashimoto's thyroiditis indicate the existence of a random distribution in both men and women and have shown an initial lag in the first few years of their life followed by a constant rate after this (Volpe et al., 1973)[42]. A few studies have suggested a slight increase in the prevalence of autoimmune thyroiditis in adolescent girls following use of iodized food products ingested to prevent iodine deficiency (Zois et al., 2003).[43]

IN INDIA

Population studies have suggested that about 16.7% of adult subjects have anti-thyroid peroxidase (TPO) antibodies and about 12.1% have anti-thyroglobulin (TG) antibodies. In this same study of 971 subjects, when subjects with abnormal thyroid function were excluded, the prevalence of anti-TPO and anti-TG antibodies was 9.5% and 8.5%.[32] In a landmark study of Hashimoto's thyroiditis in India, 6283 schoolgirls from all over the country were screened.[21] Among them, 1810 schoolgirls had a goiter. Among them 764 subjects underwent a fine needle aspiration cytology, and of these subjects, 58 (7.5%) had evidence of juvenile autoimmune thyroiditis (the term included both Hashimoto's thyroiditis and focal lymphocytic thyroiditis). Among fine needle aspiration cytology-confirmed cases of juvenile autoimmune thyroiditis, subclinical and overt hypothyroidism were seen in 15% and 6.5%, respectively.[21]

Table 1: Prevalence of autoimmune thyroiditis in goitrous girls in south India (MARWA. R. K et al,2000)[21]

Total no. Of subjects	6283	Overall prevalence of JAT
No. Of girls with goiter	1810 (28.8%)	
No. Of girls with satisfactory FNAC	764	
Prevalence of JAT	58 (7.6%)	2.1%
Prevalence of HT	43 (5.6%)	1.6%
Prevalence of FLT	15 (1.9%)	0.56%
Prevalence of JAT (n 5 722) By antibody positivity (TMA 1:1600)	51 (7.1%)	2.0%

4. Etiology

Genetic factors

In 2000, fisher G F et al[45] conducted a study on the genetic associations of Hashimoto's thyroiditis have shown that the human leukocyte antigen(HLA*)* region, which plays a major role in other autoimmune disorders, is associated with development of Hashimoto's thyroiditis. The association of Hashimoto's thyroiditis with various other autoimmune diseases has further reinforced the probable involvement of genetic factors in the etiology. The major histocompatability complex (MHC), cytotoxic T-lymphocyte association (CTLA-4) and the human

leukocyte antigen (HLA) are the genetic factors which are purported to play a major role in the pathogenesis.

MHC modulates the selection of thyroid cells in the thymus and presentation of antigens in the periphery. The sensitivity and specificity of the affinity to bind the peptides and recognize T-cells is determined largely by the genetic polymorphisms exhibited by the MHC molecule. The possible polymorphisms within the MHC molecules play a pivotal role in the predisposition to autoimmune disease. The association between the genetics of Hashimoto's thyroiditis and HLA gene loci has been investigated by sero typing the HLA, and deoxyribonucleic acid (DNA) typing the sequence- specific oligonucleotides. Different subsets of HLA genes have been found to show varying degree of associations with Hashimoto's thyroiditis in different races.

In 1994 Wu et al[46] described the association of HLA class 1 and class 2 genes both with Hashimoto's thyroiditis in Asian populations, while only HLA class 1 demonstrated the association in Caucasians. No significant associations have been found between Hashimoto's thyroiditis and HLA class 3 or non-HLA genes of the HLA region.

In 2003, Einarsdottir et al[47] noted an association between CTLA-4 and Hashimoto's thyroiditis in significant number of cases. CTLA-4 has an important role in upholding immunological self tolerance in the body and its down regulation may be the initiating step for the pathogenesis of Hashimoto's thyroiditis as well as other autoimmune disorders such as Graves' disease.

Other factors

The common environmental factors which act as triggers to initiate the insult on thyroid tissue include, selenium, cytokine therapy iodine intake and infections. In 1983, Boukis et al, demonstrated that iodine appears to be the most significant factor in initiating the disease process in animal models.[49]

PATHOGENESIS

In Hashimoto's thyroiditis, the immunologic response appears to be typically aggressive and destructive, rather than stimulatory, as in Graves' disease, Hashimoto's thyroiditis occurs in two varieties, an atrophic variety and a goitrous form The etiopathogenesis is a complex multistep process which involves various genetic, environmental and immunological factors. In a nut shell, loss of immune tolerance to normal thyroid cells leads to production of antibodies directed against thyroid

tissue, which causes the destruction of the thyroid gland. The initial disease process are triggered when genetically predisposed individuals are exposed to the above mentioned environmental factors. MHC class II antigen presenting cells, which include dendritic cells and macrophages, invade the thyroid gland. These cells present the autoantigen components of the thyroid gland to the immune system for processing

THYROGLOBULIN

TG is a 660-kda glycoprotein secreted by the thyroid follicular cells into the follicular lumen and it is composed of two identical subunits of 330 kda each. It is stored as colloid. Each TG molecule has around 100 tyrosine residues of which 25% is iodinated. These residues couple to form T3, T4. When TSH stimulates the thyroid cell, TG is taken up & hydrolyzed by lysosome. The exact location of T and B cell epitopes within TG is not known.

In 1991champion et al[50] first described the association of thyroglobulin in hashimoto's thyroiditis. found approximately 40 different types of epitopes, which play a vital role in the pathogenesis of the disease.

THYROID PEROXIDASE

Previously was known as thyroid microsomal antigen. TPO is the key thyroid enzyme catalyzing both the iodination and coupling reaction for the synthesis of thyroid hormone. 180 different types of TPO antibodies have been identified, so far. It is membrane bound protein, usually found in the cytoplasm and in high concentration on the apical microvillar surface of thyrocytes. It is of mol wt between100 to 105-kda. Anti-TPO antibodies are mainly of the igG class with igG1 and igG4 subclasses in excess.

Moreover, Studies have confirmed that even though antibodies against thyrotropin receptor and Na/I symporter have been detected in patients with autoimmune thyroid disease, they do not play a significant role in the pathogenesis of this condition.

The major step in the pathogenesis is the formation of auto reactive cells directed against the thyroid gland. This process initially occurs in the lymph nodes but as the disease progresses; it shifts to the thyroid gland where the development of lymphoid tissue follows. The stimulated B-lymphocytes produce antithyroglobulin (TGAB) and antithyroid peroxidase (ATPO) antibodies. The autoreactive T-cells infiltrate the thyroid gland and mediate destruction through cytotoxicity with the aid of

CD+8 cells. The stimulated macrophages produce numerous cytokines along with antibodies, initiate the process of tissue destruction via apoptosis. As a final step in the process, caspases induced proteolytic cleavage directly involved in the destruction of thyroid gland. The severity of the disease and the clinical outcome are determined by the rate at which apoptosis occurs in the thyroid gland. Expression of these fas proteins has direct correlation to the severity of the disease and as the rate of apoptosis increases, the mass of hormonally-active thyroid tissue decreases resulting in diminished production of thyroid hormones and more significant disease manifestations.

ETIOPATHOGENESIS OF HASHIMOTO'S THYROIDITIS (Casselman W G,1996)[48]

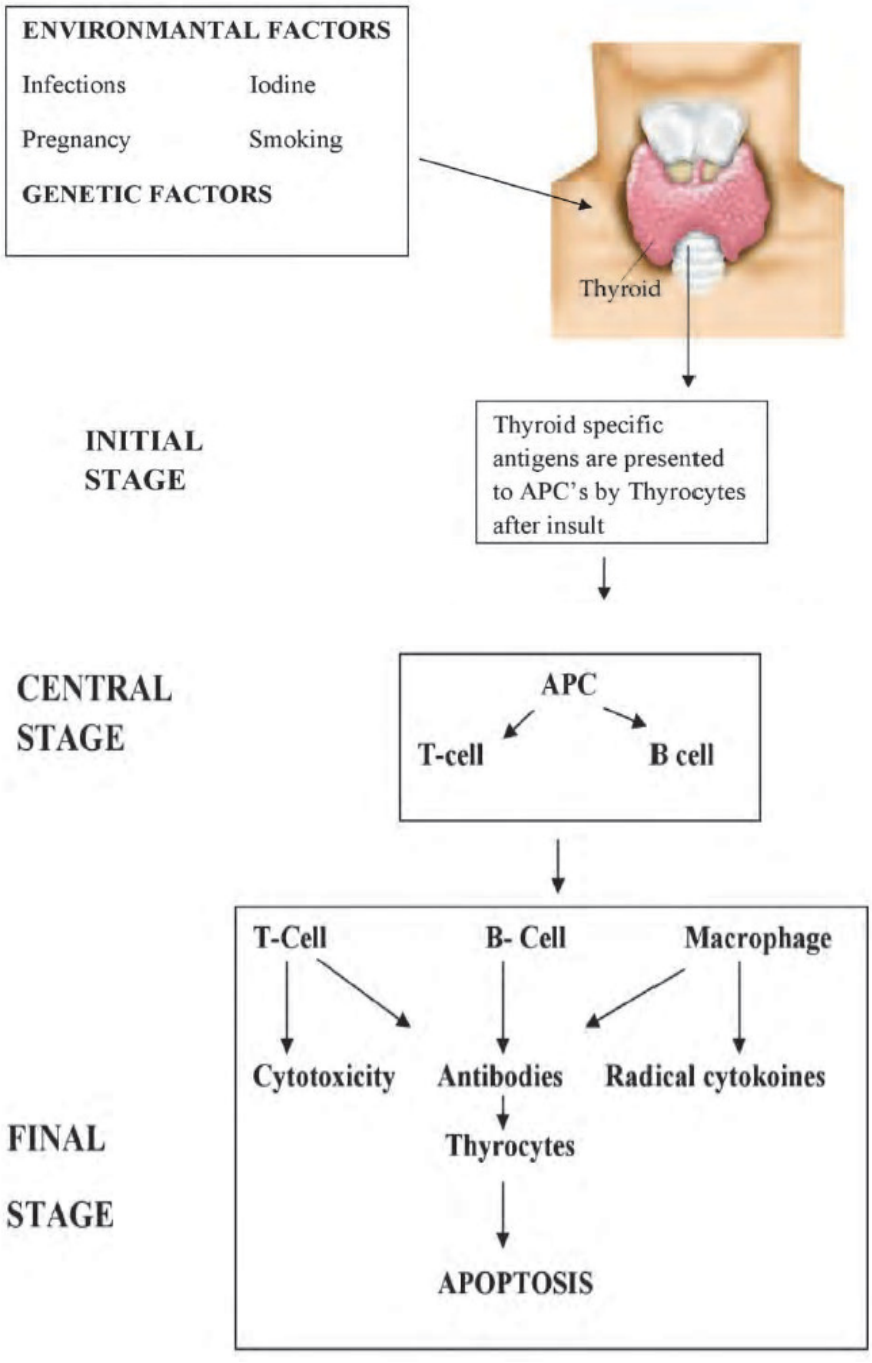


Fig 6: Etiology of hashimoto's thyroiditis

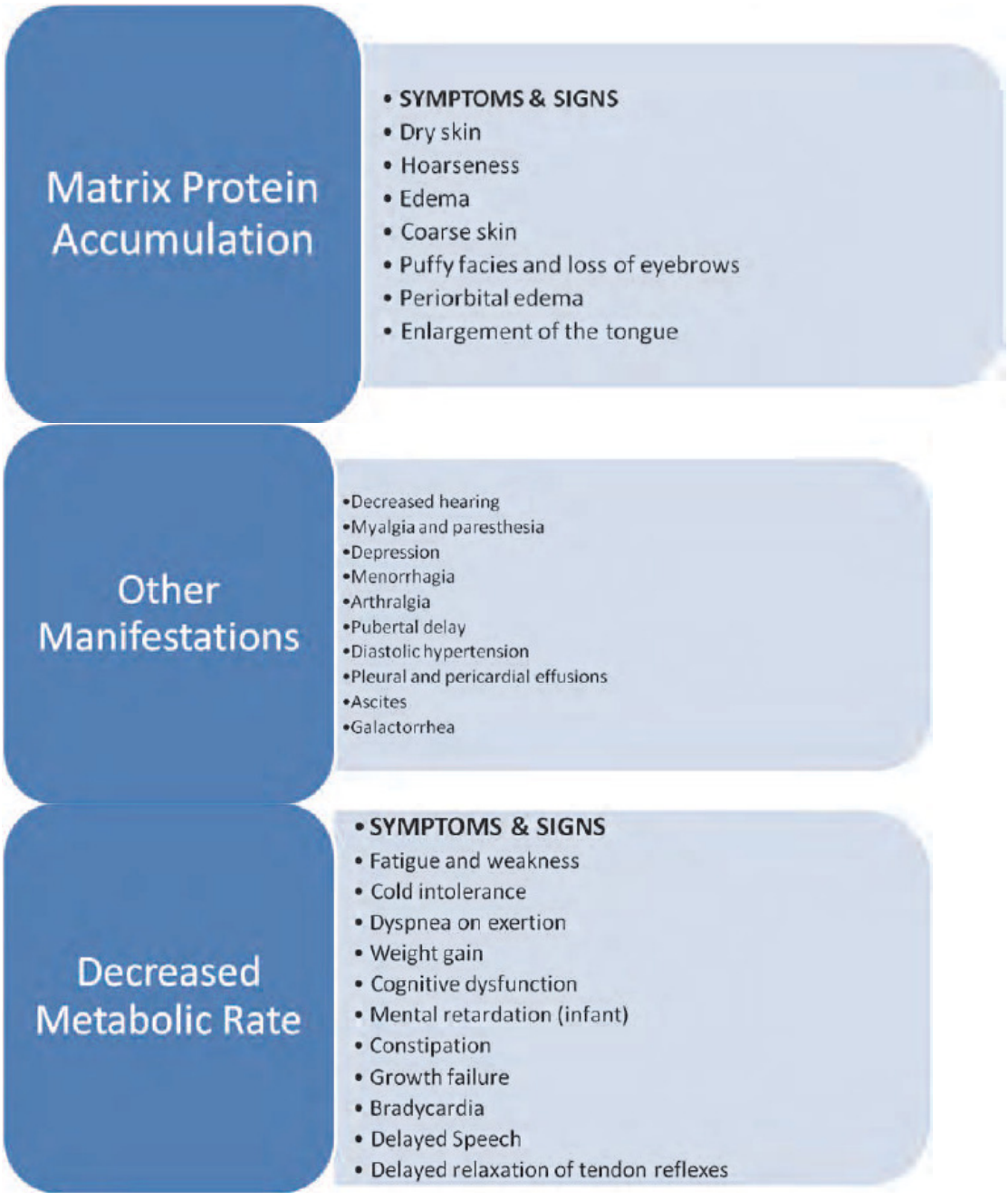
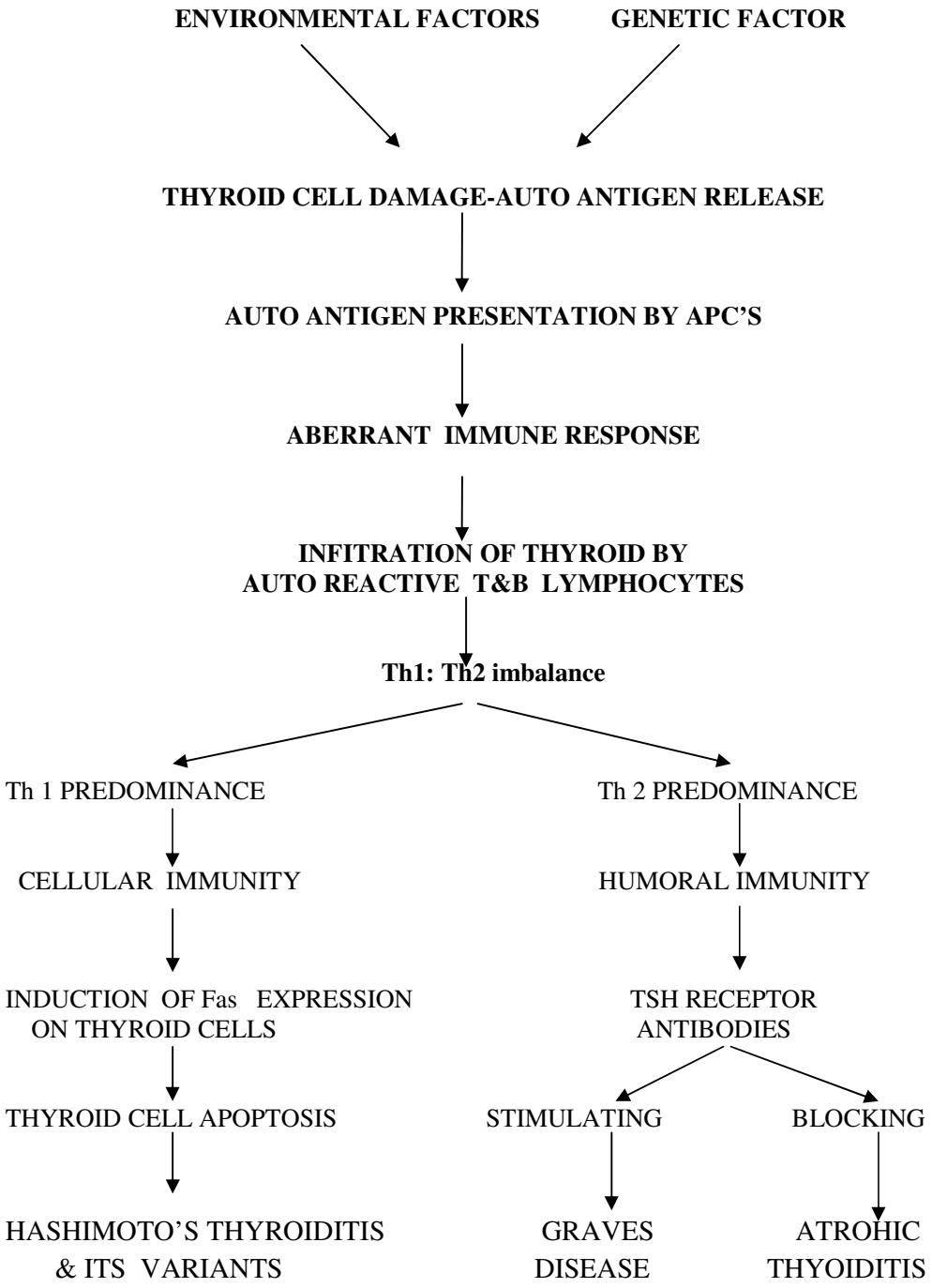
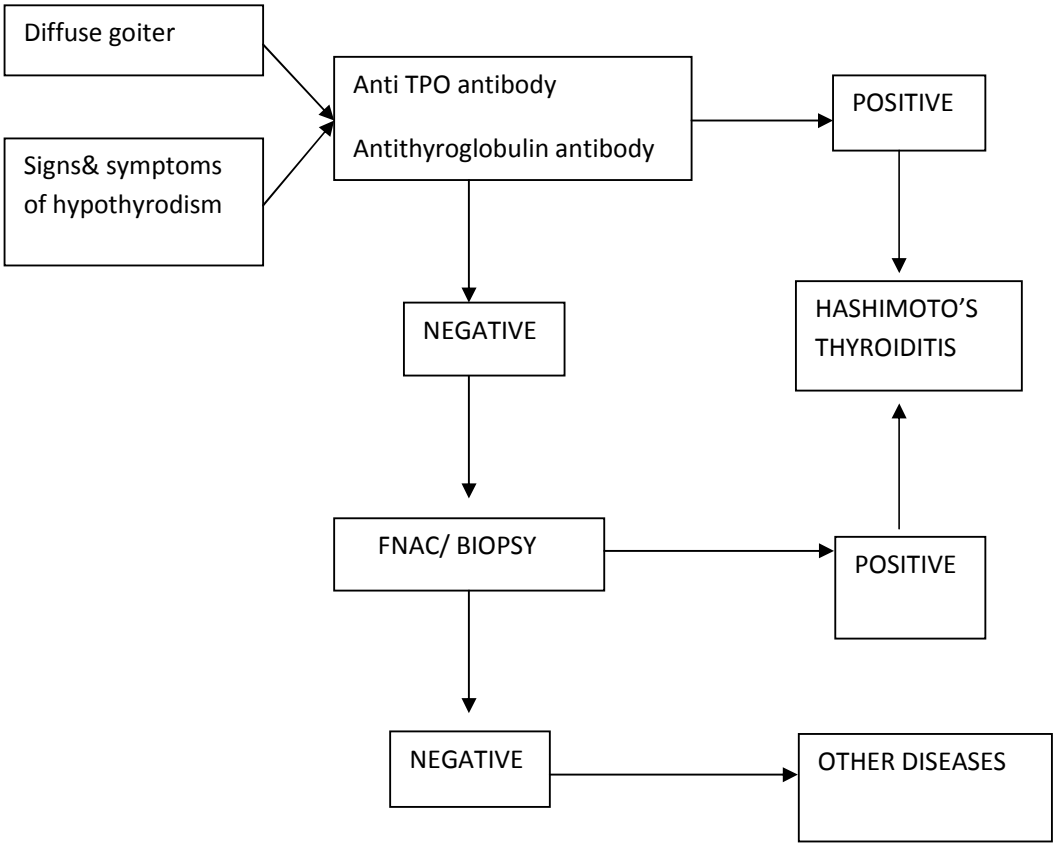


Fig 7: symptoms and signs of hypothyroidism


ENVIRONMENTAL FACTORS
GENETIC FACTOR
THYROID CELL DAMAGE-AUTO ANTIGEN RELEASE
AUTO ANTIGEN PRESENTATION BY APC'S
ABERRANT IMMUNE RESPONSE
INFITRATION OF THYROID BY
AUTO REACTIVE T&B LYMPHOCYTES
Th1: Th2 imbalance
Th 1 PREDOMINANCE
Th 2 PREDOMINANCE
CELLULAR IMMUNITY
HUMORAL IMMUNITY
INDUCTION OF Fas EXPRESSION
ON THYROID CELLS
TSH RECEPTOR
ANTIBODIES
THYROID CELL APOPTOSIS
STIMULATING
BLOCKING
HASHIMOTO'S THYROIDITIS
& ITS VARIANTS
GRAVES
DISEASE
ATROHIC
THYOIDITIS

DIAGNOSTIC APPROACH TO HASHIMOTO'S THYROIDITIS



Pathology

Hashimoto's thyroiditis represents different phases or manifestations of and organ specific immune mediated inflammatory disorder, generically designated as autoimmune thyroiditis and characterized functionally by the production of Auto antibodies that alter thyroid function. There is an immune mediated insult that leads initially to diffuse or nodular hyperactivity of the gland and eventually to exhaustion atrophy, manifested by diffuse oxyphilia of the follicular epithelium. The mechanisms leading to autoimmune thyroiditis are of both humoral and cellular nature. Circulating auto antibodies exist against thyroglobulin and other follicular cell antigens. However, it has been suggested that the initial factor resulting in autoimmune thyroiditis is an organ specific defect in suppressor T-lymphocytes is under the influence of multiple genes and is multifactorial. Grossly the typical case shows diffuse enlargement of the gland. However, in some instances, one lobe is more enlarged than the other and in others the disease has a distinctly multinodular quality. The consistency is firm but not stony hard as in Reidel's thyroiditis. There is no extension of the process outside the gland. Microscopically, the two main abnormalities are lymphocytic infiltration of the stroma and oxyphilic change of the follicular

epithelium. The lymphoid tissue is distributed within and around the lobules and it invariably exhibits large follicles with prominent germinal centers. Plasma cells, histiocytes and scattered intrafollicular multinucleated gaint cells can be present. The thyroid follicles are small and atrophic. Most of them lined by variable sized Hurthle cells. The nuclei of these cells may show enlargement and hyper chromasia. In the typical case of Hashimoto's thyroiditis, connective tissue is scanty, with slight or moderate thickening of the interlobular septa. In the fibrous variant of this disease which comprises about 12% of all cases, fibrosis is more extensive. In contrast to Riedel's thyroiditis this fibrosis is a dense hyaline type (instead of the active proliferative fibrosis seen in latter) and does not extend beyond the thyroid capsule. Although, Hashimoto's thyroiditis typically exhibits a diffuse appearance both grossly and microscopically, cases do occur in which a distinct nodularity is evident, the epithelial component of the nodules having hyperplastic quality. Hashimoto's thyroiditis has been graded pathologically as: [28,30,31]

Grade I - showing Askanization of the follicular cells and lymphocytic infiltration.

Grade II – Askanization of the follicular cells and lymphocytic infiltration with or Without lymphoid follicle formation, destruction of follicles and varying degreed of fibrosis.

Grade III - Extensive fibrosis in the gland with almost total disappearance of the follicles. This is probably the stage of burnt out disease.

Complications of Hashimoto's thyroiditis includes malignant lymphoma and Papillary carcinoma.

CLINICAL FEATURES

Hashimoto's thyroiditis is much more common in women, with a female to Male ratio of 13:1, being most commonly encountered in women at or near Menopause.[32] It is extremely rare in children, less than five years of age, but accounts for more than 40% of all goitrous enlargement with hypothyroidism in adolescents living in iodine sufficient areas.[24] Hashimoto's thyroiditis is known to run in families and is usually detected incidentally, as goitre, during a routine physical examination. Most patients are asymptomatic and when symptoms do occur, there may be an awareness of a painless anterior neck fullness. [24, 27] It is characterized by lymphocytic infiltration of the thyroid gland producing a rubbery "knobby" sometimes asymmetric swelling most

commonly resembling a multinodular goitre. It could also present as a solitary nodule or diffuse enlargement, being usually painless. occasionally, mild neck discomfort and dysphagia may be present, especially if the thyroid gland is enlarging rapidly. If the thyroid gland is sufficiently large to displace to compress the recurrent laryngeal nerve, hoarseness of voice may occur.[27] In 13% of cases, particularly in the elderly, extensive fibrosis results in an enlarging hard goitre that could be mistaken for malignancy. It is characteristically a diffuse, very firm, even hard goitre, which is often bosselated or lobulated. The pyramidal lobe could be involved as well. Regional lymph node involvement is rare, but has been described in some patients.[27]The patient usually presents with goitre in a hypothyroid state, but in about 5%of the patients, hyperthyroidism maybe the initial manifestation.[27] The classical presentation could be that of a goitre with subclinical hypothyroidism (mild elevation of TSH with normal circulating thyroid hormone levels). Extrathyroidal manifestations of Grave's disease (eg. Ophthalmopathy, dermopathy) are seen in 5to 10% of typical Hashimoto's thyroiditis.[32] The risk of developing of lymphoma is 70 to 80 times more in cases inHashimoto's thyroiditis 26 and only 5 – 10% of Hashimoto's thyroiditis end up in lymphoma. Hashimoto's thyroiditis is also prone to develop papillary carcinoma thyroid.

INVESTIGATIONS

LAB TEST FOR ASSESMENT OF THYROID STATUS – TSH, T3, T4.

The classical presentation of Hashimoto's thyroiditis could be that of goitre With subclinical hypothyroidism (i.e. Mild elevation of TSH with normal circulating thyroid hormone levels).34Hyperthyroidism occurs as an initial manifestation of Hashimoto's thyroiditis in less than 5% of the cases. Serum levels of TSH, T3 and T4 depend on the metabolic status of the patient. [27]

A raised TSH concentration and thyroid auto anitibodies are present before the Clinical features become apparent, and a raised TSH concentration could be the earliest marker for developing overt hypothyroidism. The higher the serum TSH concentration greater is the likelihood of developing overt hypothyroidism. Hence laboratory tests for assessment of thyroid status, measuring serum TSH, Total T4[42] (although free T4 is a better indicator of thyroid hormone status) and T3 are done and could be used to identify people at greater risk for developing hypothyroidism.[27]

- Normal TSH value is 0.3 – 6.0 μ IU/ml
- Normal T4 value is 4 – 13 μ g/dl.
- Normal T3 value is 70 – 200 ng/dl.

FINE NEEDLE ASPIRATION CYTOLOGY (FNAC)

Fine Needle Aspiration Cytology (FNAC) of the thyroid gland is firmly established as a first-line diagnostic test for the evaluation of goitres.[51] FNAC provides reliable distinction between a goitre and autoimmune Thyroiditis. This is important since the latter requires lifelong follow-up treatment with thyroxine to shrink the gland and to avoid the subtle decline into Hypothyroidism, which is the natural history to the untreated disease. Antibody levels and TSH estimations provide a diagnosis in 90 to 95% of cases at best. Antibodies are positive in 60 to 80% in some series, and as a smaller percentage in children and adolescents. Thus, cases may be missed if antibody estimation is used as the sole screening indicator of disease. On the other hand, antibodies may be positive in up to10 to 15% of patients without thyroiditis. A cytological diagnosis of Hashimoto's thyroiditis is valuable in aberrant clinical settings such as hyperthyroidism or where there is dual disease such as an associated neoplasm.[51]FNAC is highly accurate in the diagnosis of thyroiditis. Lymphocytic infiltration of the gland in Grave's disease may result in a overlap of the cytological appearances with Hashimoto's disease. Because thyroiditis may affect the gland focally,

diagnostic material will not be obtained in up to 10% of cases. Repeat aspirations reduce this false negative rate.[31]

Criteria for diagnosis of Hashimoto's Thyroiditis by FNAC[31]

- Oxyphilic epithelial cells (Askanazy) cells.
- Moderate number of lymphocytes and some plasma cells.
- Mulinucleate giant cells; epithelial histiocytes (variable)
- Scanty or no colloid

An abundance of lymphocytes, plasma cells and follicular cells mixed with Variable number of Hurthle cells are usually present in FNAC. The preponderance of tight clusters of mature lymphocytes is especially diagnostic. In a small group of patients the disease progresses to the fibrous variant characterized by broad fibrous bands replacing one-third or more of the parenchyma. When both the lymphoid and epithelial components of the lesions are represented in the aspirate, the diagnosis by FNAC is not difficult.

Problems in Diagnosis by FNAC [31]

1. Distinguishing bare thyroid nuclei from lymphocytes
2. Lymhocytic infiltration in or around other lesions.
3. Hashitoxicosis.

4. Lymphoma

5. Problems with Askanazy cells.

6. Unilateral or focal autoimmune thyroiditis.

7. Giant cells in autoimmune thyroiditis.

8. Proliferation of epithelial cells in florid lymphocytic thyroiditis

9. Psammoma bodies

Stripped nuclei of follicular epithelial cells resemble lymphocytes, especially when smears are poorly fixed. A thin rim of cytoplasm is characteristic of Lymphocytes and is absent around stripped epithelial nuclei. Thyroid nuclei are more evenly rounded than lymphocyte nuclei and have more homogenous chromatin and denser nuclear rim. Lymphocytes vary in size and larger, immature forms are usually also present. Blue cytoplasmic fragments (lymphoid globules) are characteristic of lymphoid tissue.[51]

In lymphocytic thyroiditis, lymphocytic infiltrate is denser than in Hashimoto's thyroiditis. Fibrosis is usually absent and thyroid epithelium usually remains intact. A lymphocytic infiltrate may be associated with neoplasia, e.g., in the diffuse sclerosing form of papillary carcinoma.[51]

In some patients with clinical hyperthyroidism, FNB yields numerous Lymphocytes. This could be the "Hashitoxic" Phase of Hashimoto's thyroiditis, which is usually transient and self-limiting, and should not be confused with cases of Grave's disease with lymphocytic infiltration.[51]

The cytological distinction between autoimmune thyroiditis and lymphoma can be difficult. Approximately 75% of lymphoma arise in a background of Autoimmune thryroiditis.[51]Pleomorphism of Askanazy cells may create difficulty in distinguishing it from Askanazy cell neoplasia. Thyroiditis should be considered if abundant epithelium and lymphocytes are Aspirated.[31]Giant cells are seen in 30% of Hashimoto's thyroiditis and together with epitheliod cells, may cause confusion with de Quervain's thyroiditis.[31]

In patients with florid lymphocytic thyroiditis, especially younger patients, Abundant active looking epithelium may be aspirated, leading to suspicion of a Neoplasm. Psammoma bodies have been described in association with Hashimoto's thyroiditis. These could also be seen in other benign processes. Their presence in smears probably warrants surgical biopsy because they are much more likely to be associated with papillary carcinoma.[31]

Antibodies

Hashimoto's thyroiditis is nearly always associated with positive antithyroid Autoantibodies, and a positive antimicrosomal antibody (AMA) can be detected in the sera of approximately 90% cases and antithyroglobulin antibodies (ATG) are detectable in about 20 to 50% of the cases.[27] It is now recognized that antithyroidperoxidase (TPO) antibodies and antimicrosomal Antibodies are in fact the same entity. Antimicrosomal antibodies are more sensitive where as antithyroglobulin antibodies are more specific in detecting thyroid autoimmune disorders. When antibodies titers were measured, in cytologically proven cases of Hashimoto's thyroidits, significant AMA titers were present in 61 of 65 patients studied. [27]

Whereas positive ATG titers were present in only 15 of 65 patients[27]. Hence, it could be said that ATG antibodies are less important than AMA in the detection of the thyroid disease. In general "non-diseased population" 6 to 8% will have detectable circulating thyroid autoantibodies. Compared with healthy controls thyroid patients were found to be more frequently positive for antithyroid antiboies.[13] It has also been noted that not all patients with Hashimoto's thyroiditis have elevated antibody levels.[31] As such it is clear that being negative for

antibodies does not necessarily exclude thyroid autoimmunity, but however when antibodies are positive, it strongly indicates the autoimmune nature of the disease.[13] It has been noticed that antibodies are detected more frequently in multinodular and diffuse goiters especially when the patients are in a hypothyroid or a hyperthyroid state.[31] It has also been seen that iodine supplementation in iodine deficient areas increases the presence of thyroid autoantibody positivity. Antithyroid antibodies rarely develop before 20years of age, but they may be a preclude to the development of subsequent hypothyroidism. Patients with high antibody titers are more prone to develop hypothyroidism after surgery and hence such patients should be left with larger thyroid remnants. Lymphocytic infiltration and positive thyroid antibodies are independent predictors for the development of postoperative hypothyroidism. The degree of lymphocytic infiltration of the thyroid gland correlates well with the antibody titres.

In about 10% of the cases, antibody titers may regress and become undetectable even without treatment. Thyroid antibodies that is both AMA and ATG could be measured by Haemagglutination methods, RIA or ELISA.[27] OthersThyroid scans demonstrate heterogeneous uptake. The iodine 123 scan usually shows diffuse, patchy uptake and in general,

provides little usefulinformation.[27] Combination of Iodine 131 and Technetium 99 scans often show discordant imaging since the former measures both iodide trapping and organification while the latter measures only trapping. Histopathology, however, remains the final answer to the diagnosis.[30]

TREATMENT

Treatment is primarily medical and even euthyroid patients with subclinical Hypothyroidism should be treated with thyroxine (100micro grams daily), and the Dose should be titrated to normalize the serum TSH. Thyroxine treatment for six Months decreases the size of the goitre by an average of 30% in 50 to 90% of cases Irrespective of initial TSH levels. It decreases the size of the goitre even in the Euthyroid patients. Serum TSH levels should be monitored at 8 to 12 weeks and then every 8 weeks until the levels are normal. After that annual monitoring is adequate. Therapy is usually life long with the likelihood of remission being only 5 to 10%.Replacement with thyroxine not only rectifies the defect in hormone Production, but also suppresses TSH thereby reducing the size of the goitre. Patients with diffuse goiters responds best to thryroxine therapy.[19 48]

Since thyroxine is the principal product of the normal thyroid gland and most T3 is produced extrathyroidally by deiodination of T4 hormone. Exogenous T3 is not Satisfactory for long term therapeutic use due to its cost and because its short half-life causes fluctuations in serum hormone levels that may exacerbate underlying heart diseases. The adequacy of the dose is determined by clinical evaluation of the patient and determination of serum levels of T4 and TSH, two or three weeks after the dose is increased. If left untreated patients with elevated TSH levels develop overt hypothyroidism at a rate of 5% per year. The goal of L-T4 therapy is normalization of serum T4 and TSH levels. Steroids are indicated (Prednisolone 20mg/day) if the goitre increases in size even with the thryroxine treatment or pressure symptoms and pain develop[52].

SURGERY

There is usually no requirement for surgery,[52] treatment being primarily Medical, as many thyroid nodules will disappear during aggressive thyroid hormone therapy. However, indications for operation in patients with suspected or established Hashimoto's thyroiditis are:[52]

- Presence of a dominant mass with incomplete regression on suppressive therapy.
- Progression of thyromegaly despite of suppressive therapy.

- History or physical findings suggestive of malignancy.
- Intermediate findings on FNAC
- Surgery is also indicated to relieve pressure symptoms due to compression

Surgery for cosmetic purposes could also be undertaken. Surgery is in the form of bilateral subtotal thyroidectomy or a Hemithyroidectomy. It is suggested that bilateral resection best relieves pressure. Symptoms and prevents tracheal compression. Postoperative hypothyroidism is common (70%) and permanent, and this rapid postoperative development to thyroid gland failure implicates surgical trauma as the inciting agent. Surgical treatment is not necessary in all cases and should be avoided if the diagnosis is definite and symptoms are mild.

MATERIALS AND METHODS

Sixty cases of Hashimoto's thyroiditis were studied from Jan. 2012 to Nov. 2012. Data was collected from sixty patients, both outpatients and Inpatients in this period, treated at Stanley medical college hospital, Chennai.

Patients were informed about the study, the relevance of the Investigations, the "non operable" treatment modality, the requirement of daily Thyroxine supplements presumably for an indefinite period of time and the Need for regular follow up.

All the investigations required for the study were usually done on an outpatient basis. Patient who underwent surgery were investigated during their admission period prior to surgery.

All Patients with goitrous enlargement referred to our endocrinological op were subjected to a hormonal assay and FNAC. If FNAC showed features of lymphocytic infiltration, then thyroid autoantibody estimation were ordered for.

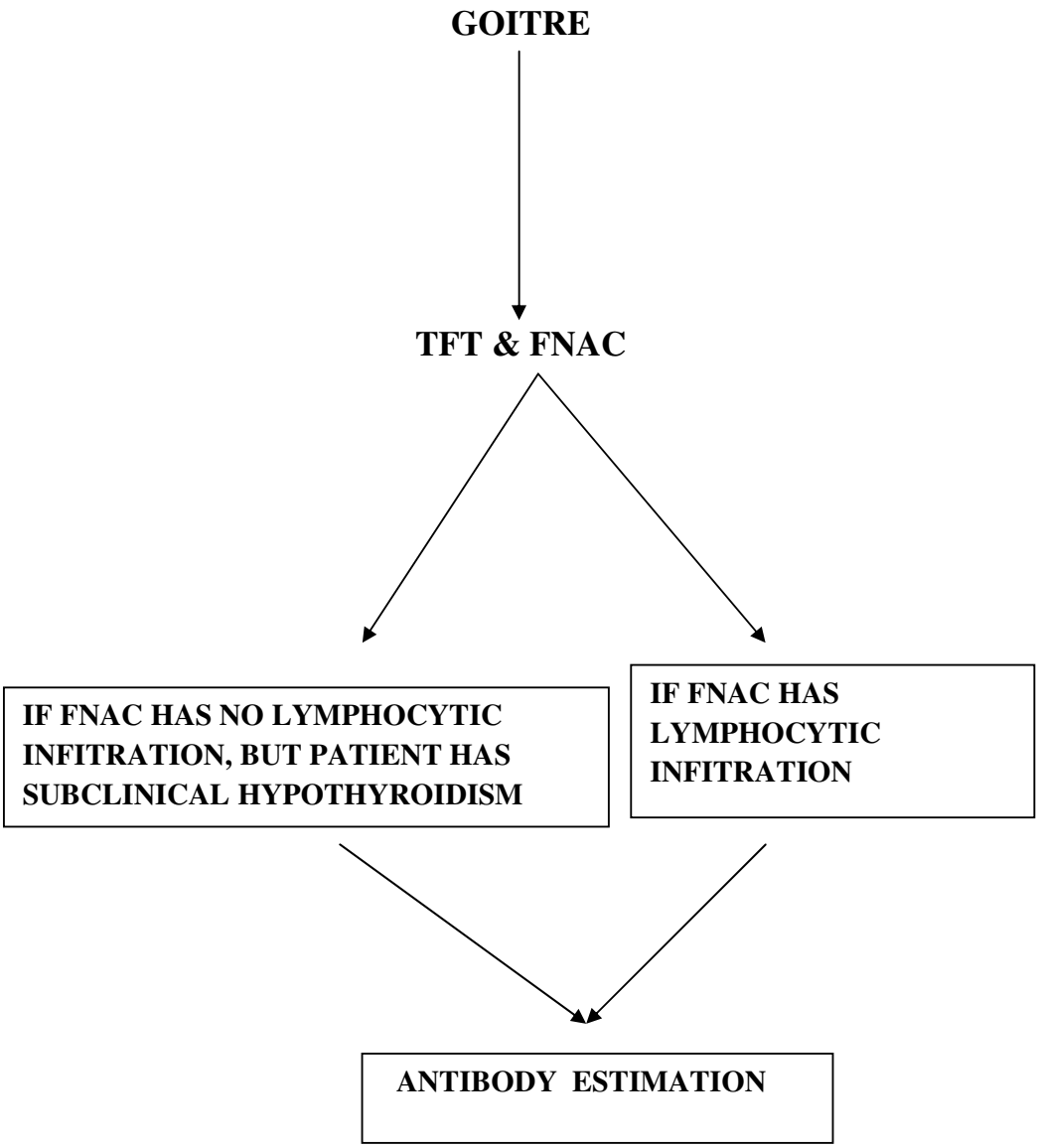
However, if FNAC showed no features of lymphocytic Infiltration, but the patient was in subclinical or overt hypothyroidism, even then

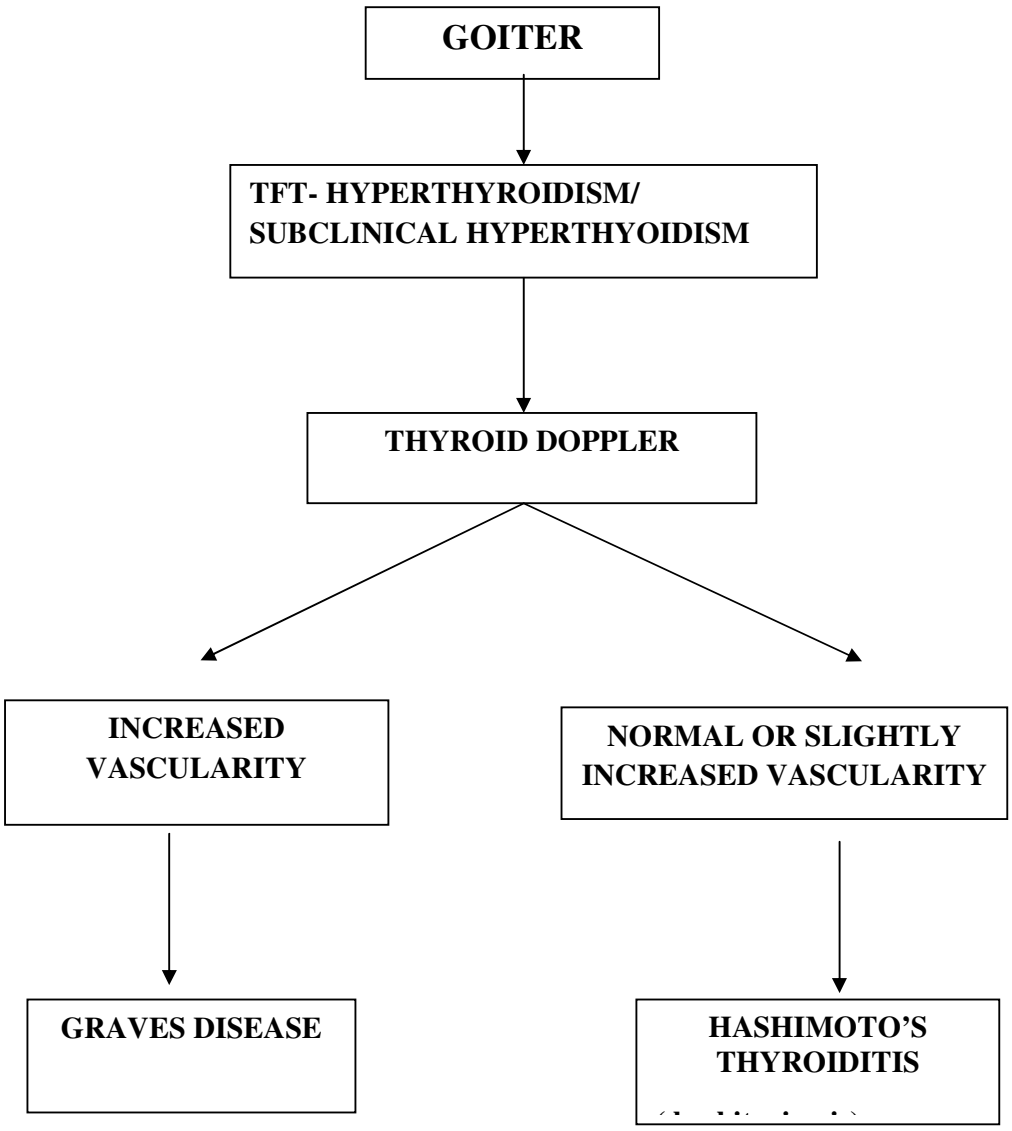
antibody estimation was done. This investigation protocol has been Figuratively represented below.

Patients,who had lymphocytic infiltration in FNAC and Thyroid function test showed hyper thyroidism/subclinical hyperthyroidism further subjected to thyroid Doppler to grade the vascularity. Thyroid colour Flow Doppler differentiates graves disease from hashimoto's thyroiditis. In hashimoto's thyroiditis, vascularity is mostly normal or slightly increased. In Graves disease, vascularity always increased.

In Patients with MNG, those who were diagnosed as hashimoto's Thyroiditis postoperatively by post op biopsy of resected thyroid specimen, also included in this study. Their symptoms & presentation were studied retro Spectively from case records and by taking history.

PROTOCOL


GOITRE
TFT & FNAC
IF FNAC HAS NO LYMPHOCYTIC INFITRATION, BUT PATIENT HAS SUBCLINICAL HYPOTHYROIDISM
IF FNAC HAS LYMPHOCYTIC INFITRATION
ANTIBODY ESTIMATION



Post operative thyroid histopathological study suggestive of Hashimoto thyroiditis also included in this study. Post-operative Histopathological examinations of the thyroid specimens were done in all cases. Immense care was taken in obtaining a detailed history and meticulous local and systemic examinations were done. The data thus obtained was recorded on a proforma prepared exclusively for the study.

AIM & OBJECTIVES

1. To study the clinical profile of hashimoto's thyroiditis patients at Stanley hospital.
2. To assess thyroid status and clinical relation in these patients.
3. To determine the demographic profile of hashimoto's thyroiditis in north Chennai population.
4. To assess the sensitivity of thyroid auto antibodies and its correlation with hypothyroidism.

INCLUSION CRITERIA

All patients diagnosed as Hashimoto's thyroiditis were included. Diagnosing could be on the basis of FNAC, positive antibody status or Final histopathology report.

EXCLUSION CRITERIA

- Patients who are not willing to get investigated in complete
- Paediatric patients
- Patients of acute thyroiditis and other causes of chronic
- Thyroiditis such as reidels thyroiditis
- Patients of previously treated cases of hashimotos thyroiditis
- Patients diagnosed as thyroid malignancies

OBSERVATIONS

During the study period sixty cases of Hashimoto's thyroiditis were treated. Out of which fifty eight were females and two male patients. These patients were studied with history, clinical signs and symptoms and investigated and recorded in the proforma. The following observations were made and they were compared with other studies.

SEX DISTRIBUTION

Table 2: sex distribution

TOTAL CASES	MALE	FEMALE
60	2	58

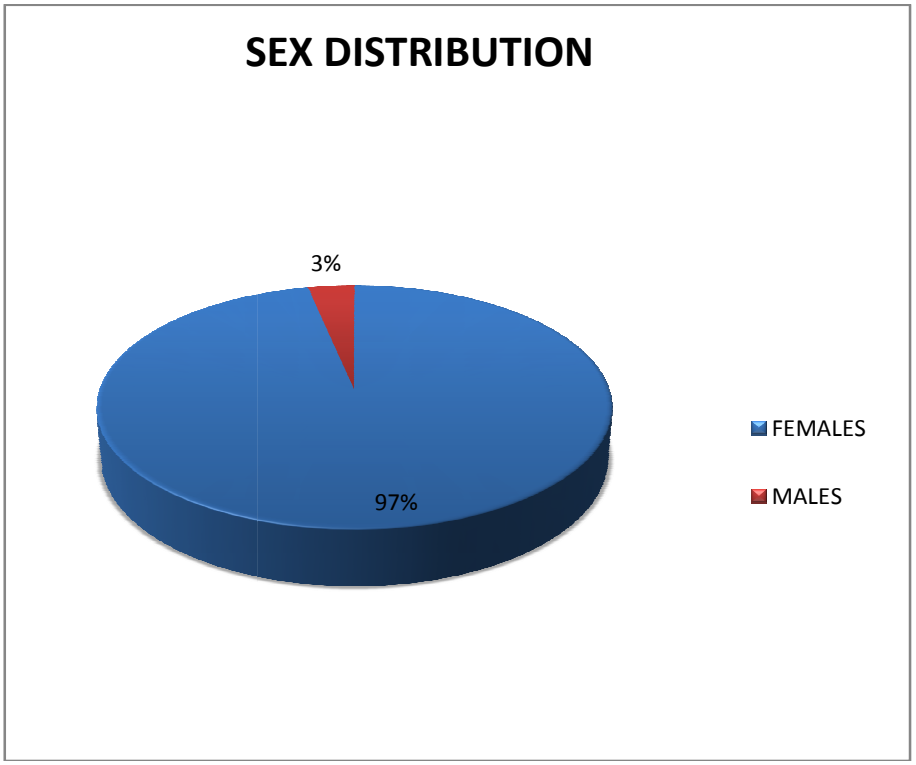


Fig 8: Graph showing sex distribution

AGE DISTRIBUTION

The age distribution of cases in our study is as follows:

Table 3: age distribution

AGE (YEARS)	FEMALES	MALES
<20	7	1
20 - 29	23	1
30 - 39	16	Nil
40 - 49	10	Nil
>50	2	Nil
TOTAL	**58**	**2**

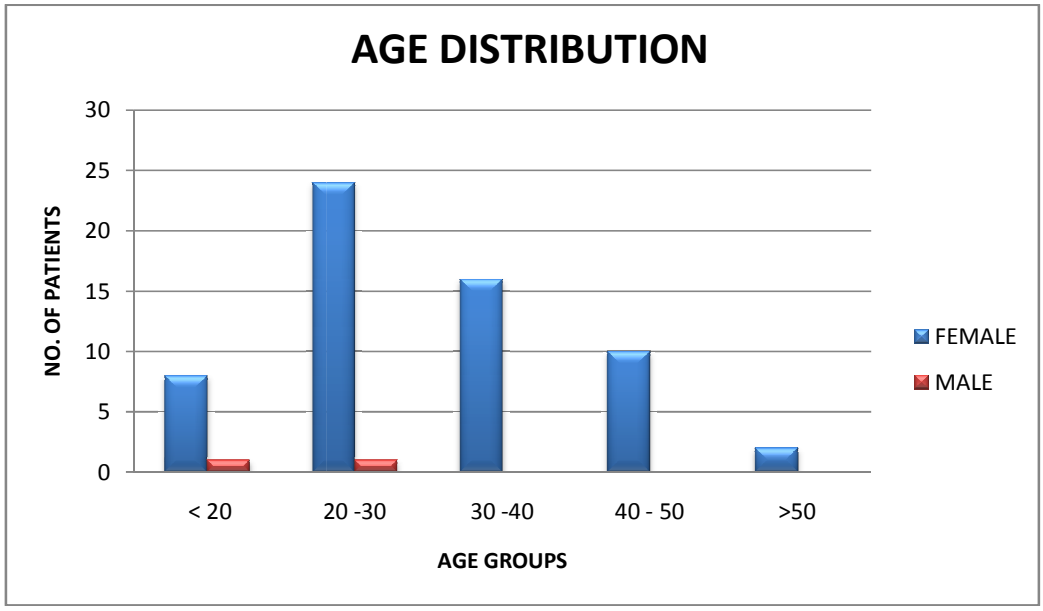


Fig 9: Age distribution

The age of the patients in this study ranged from 15– 52 years. The youngest being a 15 year old age girl and the oldest being a 52 years old woman. Most cases were in the twenty to thirty age groups. The average age of the patient in the age study being 30.46 years. The age of the two male Patients were 18 & 26.

BODY MASS INDEX & HASHIMOTO'S THYROIDITIS

Table 4: BMI in Hashimoto's thyroiditis

BMI	NO OF PATIENTS	PERCENTAGE
< 18.4	9	15%
18.5 -22.9	28	46%
23- 24.9	13	21%
>25	10	16 %

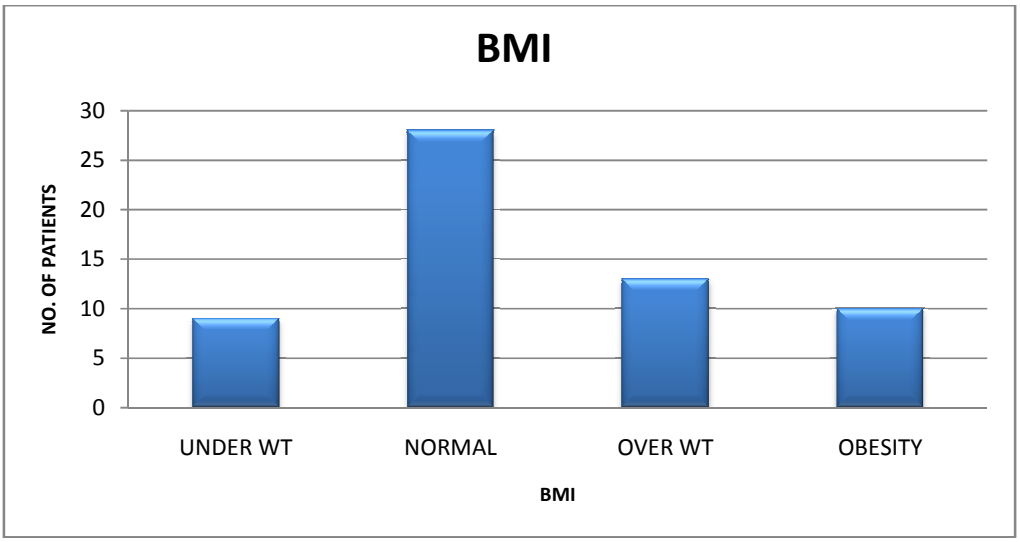


Fig 10: Graph showing BMI in Hashimoto's thyroiditis

MODE OF PRESENTATION

Table 5: Symptomatology

SYMPTOMATOLOGY	NO. OF PATIENTS	PERCENTAGE
THYROID SWELLING	60	100 %
MENNORHAGIA	12	20 %
MYALGIA	10	16.6 %
INFERTILITY	6	10 %
HAIR LOSS	4	6.6 %
TOXIC SYMPTOMS	3	5 %
OBSTRUCTIVE SYMPTOMS	2	3.3 %
FATIGUABILITY	1	1.6 %
PAIN	NIL	0

Patients with hashimoto's thyroiditis may present with out Thyroid swelling. Our study includes only goitrous patients. Toxic symptoms were like tremor, palpitations, increased sweating. No patients presented with eye signs. Majority of patients, who had myalgia as a specific symptom, were belongs to 40 to 50 age groups.

Hair loss and mennorrhagia were predominant complaint of Young women. Four patient referred to us for infertility with goitre, were found to have hashimoto's thyroiditis. Patients underwent surgery for Multinodular goitre had obstructive symptoms like dysphagia. Symptomatology of patients with other auto immune disorders were not Included, because they were not directly related to thyroiditis.

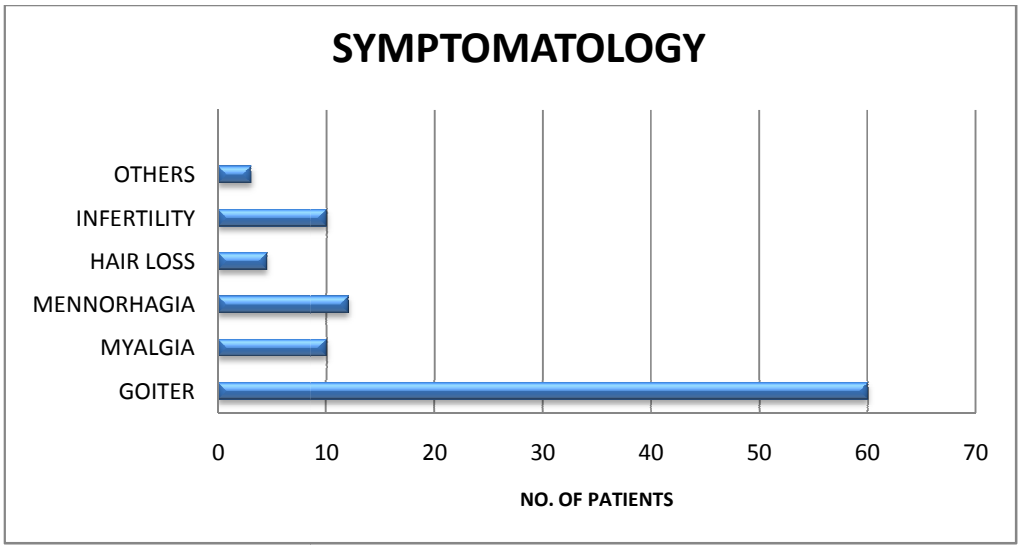


Fig 11: symptomatology

CLINICAL PRESENTATIONS

Table 6: clinical presentation

CLINICAL PRESENTATION	NO. OF PATIENTS	PERCENTAGE
DIFFUSE GOITER	54	90 %
MNG	4	6.6%
SOLITARY NODULE	2	3.3%

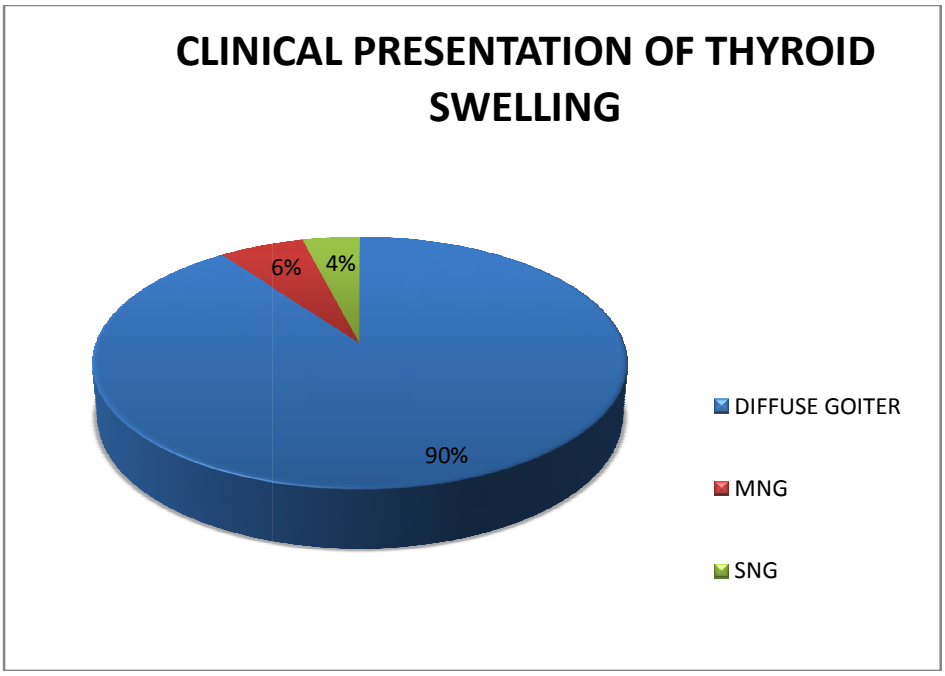


Fig 12 : Graph showing clinical presentation

Fig 13 :Multinodular goitre

Fig 14: Diffuse goitre

Fig 15:Male patient with hashimoto's Thyroiditis (diffuse goitre)

Fig 16:female patient with hashimoto' thyroiditis(SNG)

DURATION OF SWELLING

Table showing duration of swelling:

Table 7 : duration of the swelling

DURATION OF SWELLING	NO OF CASES	PERCENTAGE
0 – 3 MONTHS	19	31%
3 – 6 MONTHS	26	43%
6 mths – 1 year	13	21%
– 2 years	2	3%
>2 years	NIL	0

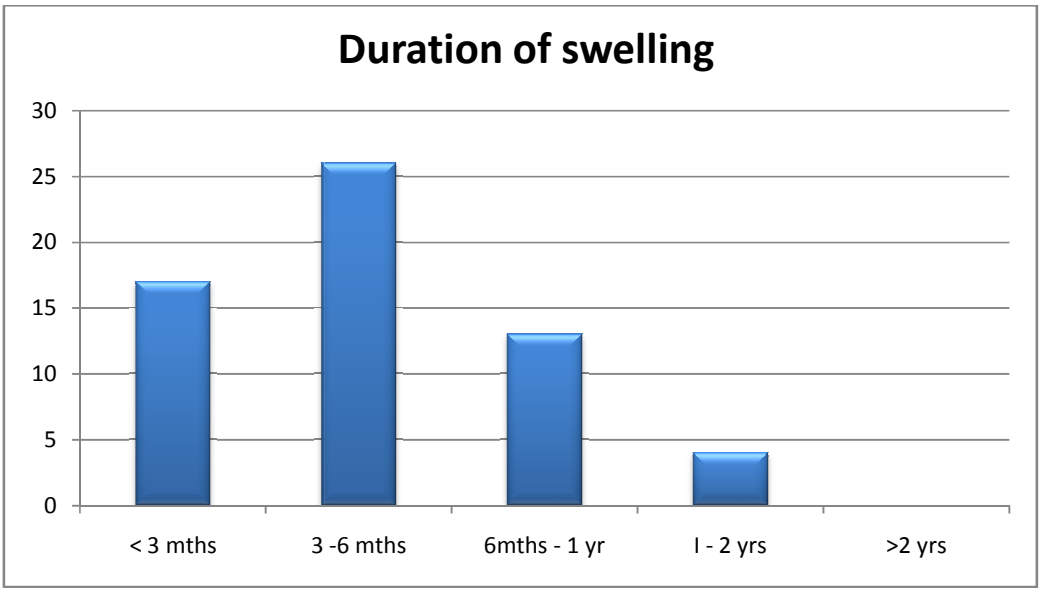


Fig 17: Graph showing duration of swelling

Average duration of the thyroid swelling was 4.5 months most of the patients fall between 3-6 months. 31 percentage of the patients were Not aware of thyroid swelling. The neck swelling noted by their relatives Incidentally 10% of goitrous patients referred from government organized Screening camps.

Nobody had pain over thyroid swelling few of them had abnormal vague throat discomfort. Maximum duration of thyroid swelling noted in this study were one and half years in 2 patients. They presented with Multinodular goitre and underwent surgery for obstructive symptoms.

Minimum duration of the swelling was 1 month. 7 patients had this short duration. They were not aware the swelling. They do not have any other specific symptoms.

THYROID STATUS AT PRESENTATION

Thyroid profile for estimation of TSH, T3 and T4 were done in all sixty Patients. The results are as follows:

Out of the SIXTY cases nineteen patients had hypothyroidism, seven cases had hyperthyroidism and fourteen patients were euthyroid.

Table 8 : Thyroid status in hashimoto's thyroiditis patients

THYROID STATUS	NO. OF PATIENTS	PERCENTAGE
EUTHYROID	30	50 %
HYPOTHYROID	5	8%
SUBCLINICAL HYPOTHYROID	13	21 %
HYPERTHYROID	3	5%
SUBCLINCAL HYPERTHYROIDISM	9	15 %

Only eight percentage of patients had hypothyroidism. Fifty percent of patients were euthyroid. Nine percentage of patients had subclinical hyperthyroidism that is TSH is very low or undetectable and Clinically asymptomatic. Their free T3 & T4 were normal.

Subclinical hypothyroidism found in 13 patients. Hyperthyroidism was present in 3 patients . These patients further subjected to colour floe Doppler of thyroid to differentiate it from graves disease. These Patients did not have opthalmopathy.

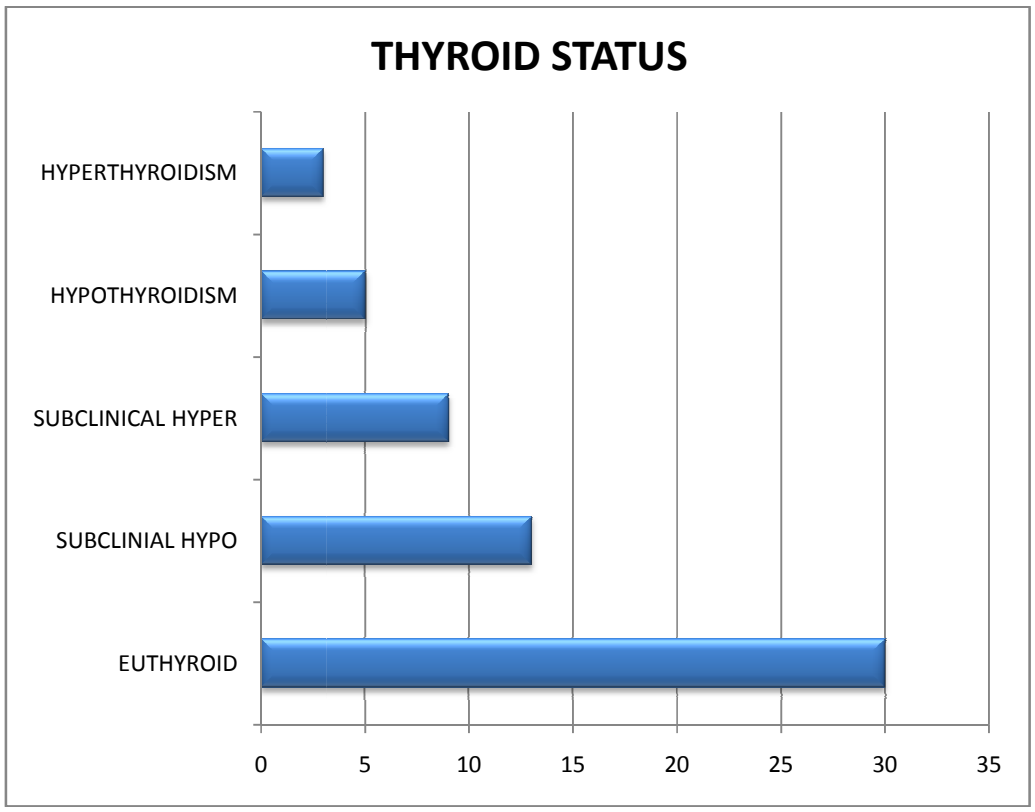


Fig 18 :thyroid status in hashimoto's thyroiditis patients

ANTIBODIES AT PRESENTATION

All sixty patients had their thyroid Autoantibody Estimation done. Antibody estimations were done by haemagglutination Methods. 92 % of the patients showed auto antibody positivity.

Table 9 : Antibody level in hashimoto's thyroiditis patients

ANTIBODIES ESTIMATION	No. of patients	Percentage
BOTH POSITIVE	41	68 %
BOTH NEGATIVE	5	8 %
ONLY TPO Ab	11	18%
ONLY Tgb Ab	3	5%
No of pts positive for TPO	52	86 %
No pts positive for Tgb Ab	44	73 %

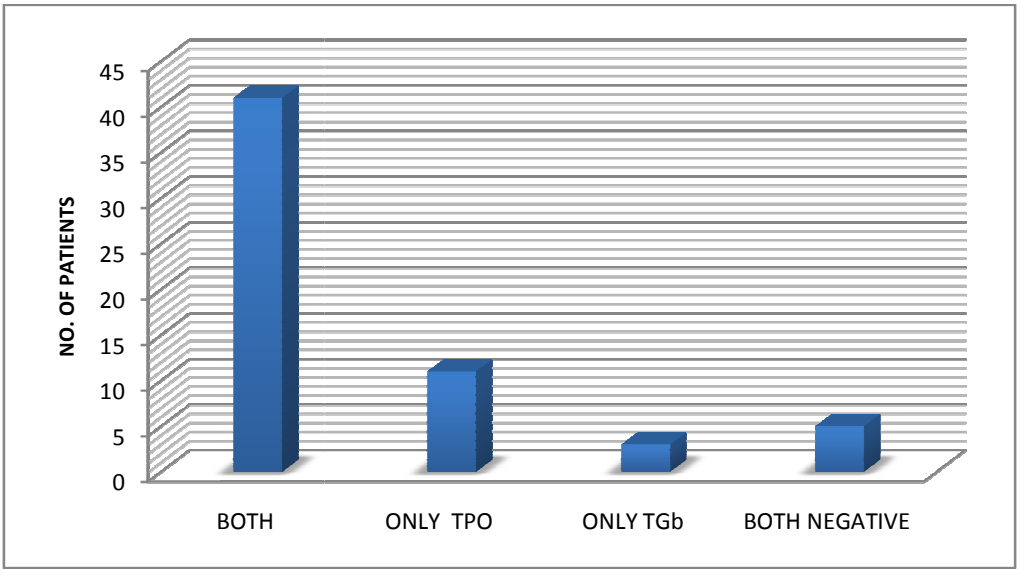


Fig 19 : Graph showing antibody levels in hashimoto's patients

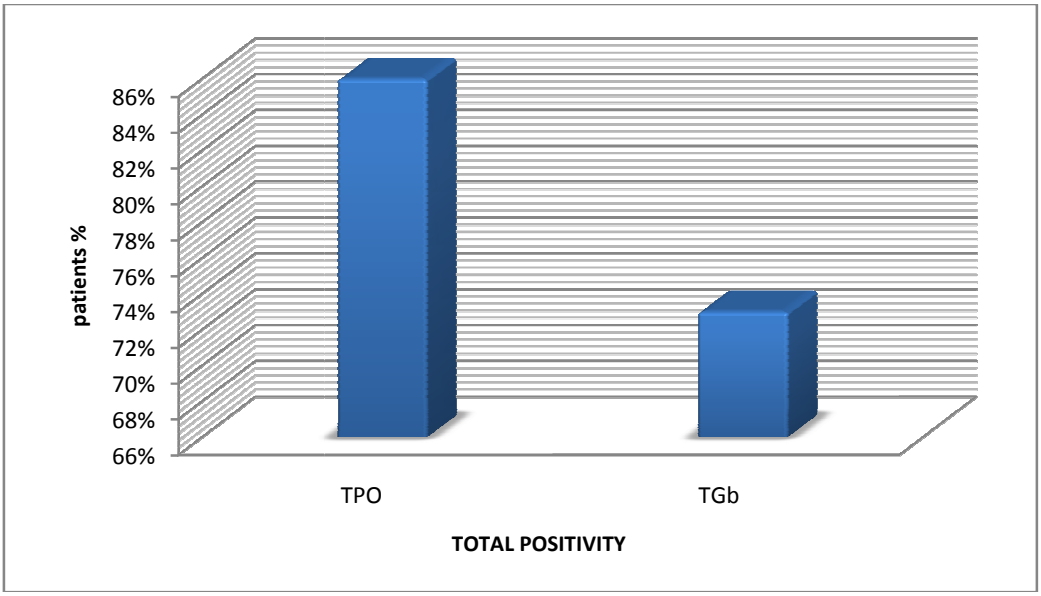


Fig 20: sensitivity of anti TPO & TGb antibodies

Anti TPO antibody present in 57 patients (94%). Anti thyroglobulin antibody present 49 patients (81%). Both were positive in 76% of the patients.

Anti TPO level in young patients just above reference range. Anti TPO level also high in hypothyroid patients. That means anti TPO levels correlates with severity of the disease. Average anti TPO level in hypothyroid patients is 85 units. Anti thyroglobulin levels does not correlate with severity.

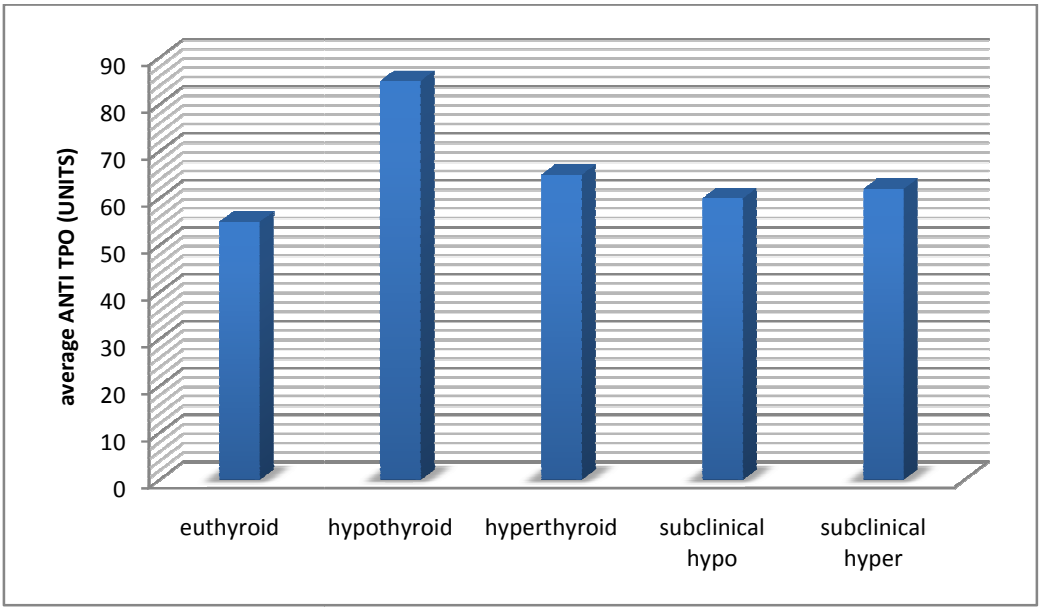


Fig 21: Average Anti TPO in Study Population

ANA POSITIVITY IN HASHIMOTO'S THYRODITIS

Table:10 ANA positivity in Hashimoto's thyroiditis patients

ANA	NO OF PATIENTS	WITH SLE	PERCENTAGE
1:40 DILLUTION	14	NIL	23 %
1:160 DILLUTION	1	1	1.6%

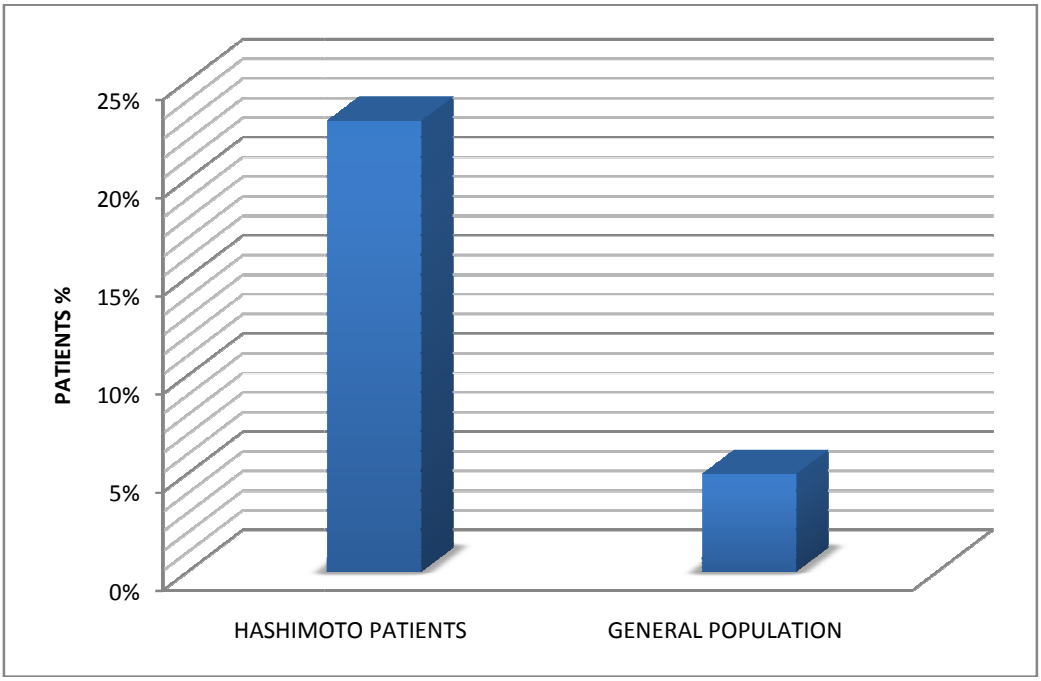


Fig 22: ANA Positivity

ANA positive in 23 % patients in very low titer (1:40). These patients referred to rheumatology OPD for further evaluation. Anti dsDNA negative in this Patients. They did not have other symptoms or signs suggestive of lupus.

STUDY	NO OF PATIENTS	PERCENTAGE
Tektonidou et al 2004[52]	58/168	35%
Our study	15/60	24%

ULTRA SOUND IMAGING IN HASHIMOTO'S THYROIDITIS

Table 11: USG findings in Hashimoto's thyroiditis patients

USG FINDINGS	NO OF PATIENTS	PERCENTAGE
HETROGENOUS ECHOTEXTURE	60	100%
DIFFUSE HYPOECHOGENECITY	56	93 %
NODULARITY	8	13 %
CALCIFICATION	NIL	0 %
THYROID VOLUME >14 CC	6O	100 %
LYMPH NODES	NIL	0%

FIG 23 : USG THYROID – right lobe of thyroid showing diffuse echohgenecity with hetrogenous echotexture.

FNAC FINDINGS

All forty patients underwent FNAC and all of them had cytopathological diagnosis of Hashimoto's thyroiditis was made.

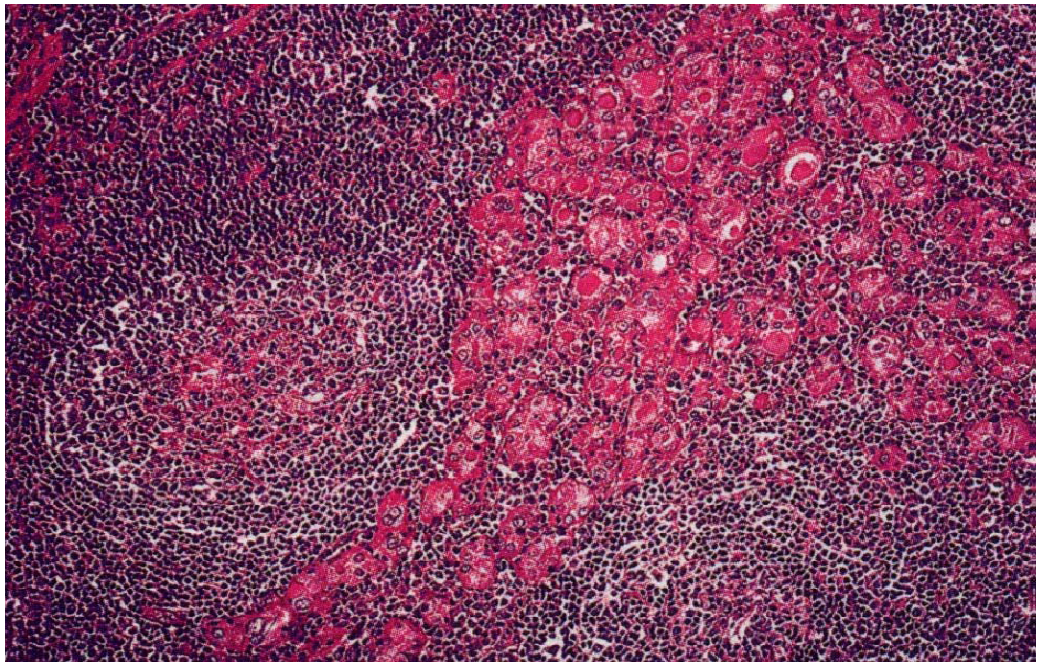


Fig 24 : FNAC showing lymphocytic infiltration & atrophic follicles

ASSOCIATED WITH OTHER DISEASES

Table 12: associated diseases

DISEASE	NO OF PTS	PERCENTAGE
SLE	1	1.6%
TYPE 1 DM	3	5%
TYPE 1 RTA	1	1.6 %
VITILIGO	4	6%

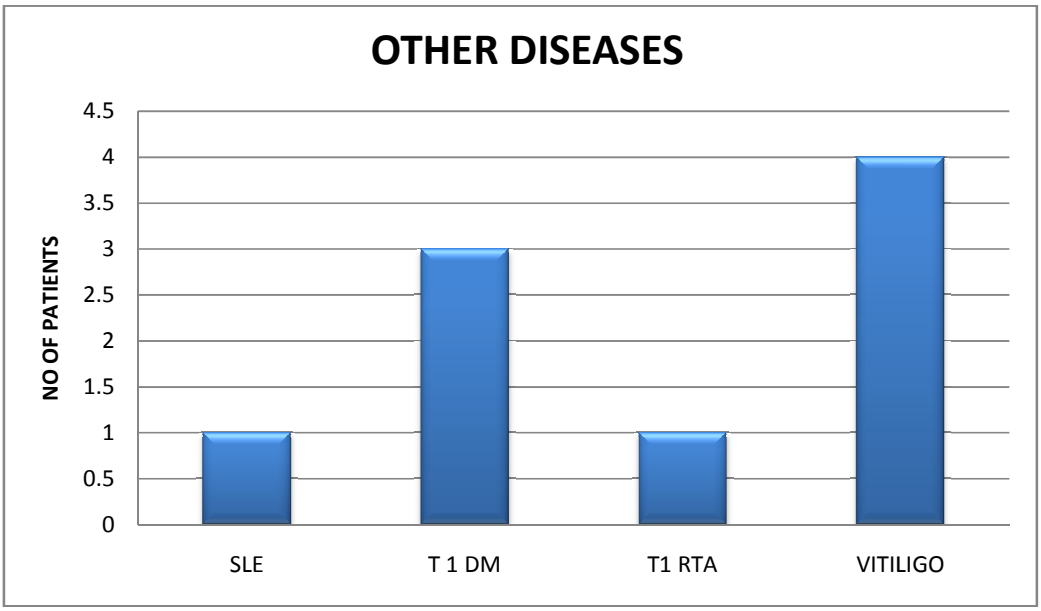


Fig 25 : other diseases

Vitiligo is the most common auto immune disease associated with hashimoto's thyroiditis, next common is type 1 DM. we had 4 vitiligo patients. 3 patients had segmental vitiligo,one had generalised vitiligo. There is no assocxiation established between AITD & type 1 RTA. Only three case reports available in literatures.

Anemia is common finding in our study. 34 patients had anemia. 29 patients had microcytic, hypochromic pciture in peripheral smear and reticulocyte count less than 2%.

CLINICAL AND LABORATORY FINDINGS

CLINICAL / LABORATORY FINDINGS	EUTHYROID	HYPOTHYROID	SUBCLINICAL HYPOTHYROID	SUBCLINICAL HYERTHYOID	HYPERTHYROID
NO. OF CASES	30	5	13	9	3
DIFFUSE GOITER	24	5	13	9	3
MNG	4	-	-	-	-
SNG	2	-	-	-	-
BOTH AB POSITIVE	17	4	9	8	3
ONLY TPO	8	-	2	1	-
ONLY tgb	1	1	1	-	-
ANA POSITIVE	8	1	4	0	1
NORMAL BMI	19	-	3	5	1
UNDER Wt	3	-	-	4	2
OVER Wt	3	3	7	-	-
OBESE	5	2	3	-	-
OTHER AUTOIMMUNE DISORDER	Gen. vit -1	SLE-1,T1DM-1 T1RTA-1,VIT -2	T1DM-2, VIT -1	-	-
ANEMIA	8	5	13	7	1
HYPER CHOLESTREMIA	3	4	2	-	-

Table 13 showing patients clinical presentation and laboratory findings:

DISCUSSION

During the study period from April 2012 to November 2012, sixty patients were detected to have Hashimoto's thyroiditis either by FNAC, antibody titers or final histopathology reports. Female preponderance is a well established feature of thyroid diseases and our study was no different having a strong female preponderance with 58 females and 2 male patients, the male to female ratio being 29: 1. This coincides with the other observations.

Table 14: comparison of sex ratio

STUDY	MALE: FEMALE RATIO
Joseph et al, 1967[22]	1:12
Fenn et al, 1980[23]	1:14
Sharma et al, 1990[24]	1:13
Gopalakrishnan et al, 2008[25]	1:40
Siriwera et al 2010,[26]	1:10.3
Skarpa et al 2011,[27]	1:40
Our study	1:29

Age distribution

Our study the age incidence ranged from 15 years to 52 years, the youngest being a 15 years old girl and oldest being a 52 year old woman. The average age in this study was 30.45 years and highest incidence being in the 20-30 year age group.

Table 15: comparison of age distribution

Study	Age distribution
Laskmana rao et al[28]	Average age 40.4
Fenn et al[23]	40 – 50 years
Siriweera et al[26]	50 – 60 years
Staii et al[29]	40 -50 years
Our study	20- 30 years average age 30.3

According to various studies, distribution disease is more prevalent among 40 - 50 years. In our study, the age distribution shifted to 3 rd decade, which is not observed in other studies. This is probably due to increased awareness about thyroid disease in north Chennai population, who reports to the clinic for even minimal thyroid swelling. The demographic profile of hashimoto's thyroiditis in north Chennai population, is entirely different from others countries. The role of iodine as trigger factor of hashimoto's throiditis is mention in several, which is not statistically proven. But still high iodine content food intake can

precipitate thyroiditis in a genetically predisposed individual. Iodine content in ground water & drinking water is very high and fish is the staple diet in this pupils. This may be the probable cause of early occurrence of the disease in this population. As the disease is more prevalent in younger age group and patients who develop the disease before child birth, most often develop infertility. It is not observed in other studies. 6 patients referred to our endocrinology opd for infertility evaluation, diagnosed as hashimoto's thyroiditis.

Duration of the thyroid swelling

All the patients presented with a history of swelling in front of the neck, 3Patients with additional features suggestive of hyperthyroidism and two patients presenting with the additional features of obstruction. All the goiters were were firm in consistency. Average duration of the thyroid swelling was 4.5 months. Most of the patients fall between 3-6 months. 4 patients had multinodular goitre. 2 patients had solitary nodular goitre. We evaluated only goitrous patients, so all patients in this study had goitre. Duration of goitre varies between 1month to one and half years. Most of the studies describe that it varies from 1 year to 4 years. In our study, no patient had swelling more than two years. This is because of earlier presentation to the physician probably due to increased awareness

about thyroid related problems in the community. Most of the patients (30%) not aware of the swelling. Thyroid swelling was noticed incidentally by their relatives. Nobody had pain over thyroid swelling. Few patients complained vague throat discomfort

Table 16: Comparison of type of Goiter

STUDY	DIFFUSE GOITRE	MNG	SOLITARY NODULAR
Kusum Kapila et al[30]	55%	18%	25%
Amani et al[31]	60%	0	40%
Siriweera et al[26]	84 %	10 %	6 %
Our study	90 %	6.6%	3.3%

In our study majority of the patients presented with diffuse goitre compared to other studies. In general, multinodular goitre rules out hashimoto's thyroiditis. However, hashimoto can coincide with multinodular goitre. Multinodular goitres mostly euthyroid and more than half of the patients with hashimoto's thyroiditis are asymptomatic .so hashimoto's thyroiditis is diagnosed in MNG by routine post thyroid specimen histopathological studies. In this study, hashimoto 's thyroditis associated with MNG found in 4 patient. Two patients were diagnosed post operatively. They all were euthyroid. In retrospective study conducted in srilanka in 2010 by Siriweera et al showed 10 % of the

hashimoto ‘s thyroiditis associated with multinodular goiter. Iodine deficiency is one of important factor for development of multi nodular goiter. Since north Chennai is an iodine sufficient area, MNG are not commonly seen as other parts of India. This may be cause of very low association of MNG in hashimoto’s thyroiditis in our study.

Thyroid status

Hashmoto’s thyroiditis is mostly clinically asymptomatic. 75% of patients are euthyroid during early presentation. Around 20% are hypothyroid. 5% are hyperthyroid. Data regarding subclinical hypothyroidism & hyperthyroidism are not extensively studied. In our study 50 % were euthyroid, similar to other studies.

Table 17: Comparison of Thyroid Status with various Studies

Study	Euthyroid	Hypothyroid	Hyperthyroid	Subclinical Hypothyroid	Subclinical Hyperthyroid
Fenn et al[23]	46.6 %	44.44%	6.6%	-	-
Kusum Kapila et al [30]	79.3%	10.10 %	6.9%	-	-
Unnikrishnan et al [32]	78 %	6.5%	-	15%	-
Butt et al [33]	83%	7.6%	9.5%	-	-
Marwaha et al[21]	79%	2.3%	0	18.6%	0
Svenson et al [35]	39%	14%	-	47%	-
Demirbilek et al [36]	43.2%	21%	-	24%	-
Skarpa et al [26]	57%	8%	-	32.9%	-
Corrias et al [37]	53%	43.6%	-	-	-
Our study	50%	8%	5%	21%	15%

The hypothyroid and euthyroid patients in our study accounted for 8 % and 50% respectively, while the hyperthyroid patients accounted for 5% of the cases.

Hypothyroidism

As the age advances, incidence of hypothyroidism increases in our patients. It also correlates with duration of swelling.

Table 18: no. of hypothyroid patients in various age groups

Age groups	No of Hypothyroid pts
<20	1
20-30	-
30-40	2
40-50	5

Table 19: duration of goiter & hypothyroid patients

Duration of swelling	No. Of hypothyroid pts
<3 months	0
3-6 months	3
6- 12 months	5

Correlation between no of hypothyroid patients and duration of swelling probably due ongoing destruction of thyroid gland & loss of follicular cells.

Incidence of subclinical hyperthyroidism is very high in our study comparing to other studies where subclinical hyperthyroidism not detected in their observations.

Subclinical hyperthyroidism & hashimoto's thyroiditis

In early stages of hashimoto's thyroiditis, thyroid hormones will leak from damaged follicles. Around 5 % patients develop signs of hyperthyroidism. Some patients don't develop toxic symptoms .but their TSH will be low (sub clinical hyperthyroidism).

Hashitoxicosis

Toxic symptoms found in 5 patients. Hashimoto's thyroiditis with toxic symptoms known as hashitoxicosis. It can be differentiated from graves disease both clinically & by using colour flow Doppler. Opthalmopathy usually associated with graves disease .it is uncommon in hashitoxicosis. Thyroid vascularity increased in graves disease, will be normal or slightly increased in hashimoto's thyroiditis.

Subclinical hypothyroidism

In our study, subclinical hypothyroidism noted in 21% patients next to euthyroid state. Most of the patients were in younger age groups. Youngest patient was 18 year old. Elder is 45 years. 6 patients referred infertility evaluation. This accounts for 10% of the total patients.

THYROID AUTOANTIBODIES

In our series, 92% patients had thyroid autoantibodies positive. The series of Hasanat et al[13] and Lakshamana Rao et al[20] reported thyroid auto antibodies Positivity of 63% and 83.34% respectively.

Hansant et al showed autoantibody positivity of 55% and 37% in their hypothyroid and hyperthyroid groups respectively. Both antibodies positive in 76% patients. 94% of the patients had TPO anti bodies. 81% had thyroglobulin antibodies.

Table 20: Comparison of antibody positivity[21,38]

Study	Study population	TPO antibodies	Thyroglobulin antibodies	Both positive
Marwaha et al, 2000	43	29 (67.4 %)	18(41.8 %)	17 (39.5 %)
Jayaram et al 2005	88	81(93%)	73 (83%)	_
Our study	60	57 (94%)	49 (81%)	46 (76%)

Table 21: comparison of anti TPO Ab sensitivity

Study	Sensitivity of anti TPO Ab
Hassanat et al[21]	63%
Lakshmana rao et al[28]	83%
Marwaha et al[21]	94%
Jayaram et al [38]	92%
Our study	94%

In this study FNAC was positive in all patients, in sharp contrast to the observation made by Lakshmana Rao et al[20] who with a 14-16 gauge needle achieved an accuracy of 77.70%. Other studies showed more than 90 % sensitivity.

The patients were followed up regularly at intervals of 3 months, and at every visit the pulse, weight, consistency of the gland and diameter of the neck were recorded. All the hypothyroid and euthyroid patients were put on thyroxine replacement and thyroxine suppression therapy respectively and monitored clinically. Eventually all the patients were found to be clinically euthyroid. All the patients with diffuse goiters and solitary nodules put on hormonal therapy with thyroxine showed a decrease in size of the gland that was appreciated bimanual palpation and by measuring the girth of the neck. The patients with multinodular goiters showed no increase or decrease in size of the gland.

SUMMARY

Sixty patients were diagnosed to have Hashimoto's thyroiditis in the study period from Jan. 2012 – Nov 2012. The study was conducted at Stanley medical college, Chennai.

The findings of our study were compared with that of the available literature.

The findings of our study are as follows:

1. The occurrence of Hashimoto's thyroiditis was maximum in the 20-30 year age group.
2. Females outnumbered the males with a male to female ratio of 1: 29.
3. All the sixty patients presented with complaints of swelling in front of the neck. Two patients presented with obstructive symptoms as well.
4. Duration of the swelling ranged from 1 month to one and half years, however, most of the patients presented within 6 months of noticing the swelling.
5. Consistency of the gland was firm in all cases.

6. In our study, 4 patients were multinodular goiter (6.6%), 54 were diffuse. Goiters (90%) and 2 was solitary nodule (3.3%).

7. 5 patients were hypothyroid (8 %), 30 patients were Euthyroid (50%) and 3 patients were hyperthyroid (5%). 13 patients had subclinical hypothyroidism (21%), 9 patients had subclinical hyperthyroidism (15%).

8. FNAC was positive in 60 patients (100 %).

9. Antibodies were positive in 55 patients (92 %).

10. Anti TPO antibody levels also correlates with severity of the disease. average anti TPO level in hypo thyroid patients is 85 units which is significantly higher than euthyroid patients. Anti thyroglobulin levels does not correlates with severity.

11. ANA (1:40 Dillution) positive in 14 (23%).

12. 46% patients had normal BMI. 21% of the patients were over weight. 15% were under weight. 16% were obese.

13. 28 patients were treated conservatively and monitored regularly every 3 months. Eventually, at the time of writing this article, all 28 patients were clinically Euthyroid. All diffuse goiters and solitary nodules regressed in size with Thyroxine therapy. The multinodular

goiters showed no increase or decrease in Size of the gland. All but two patients were treated conservatively. Two patients underwent surgery for Obstructive symptoms histopathology revealed to be Hashimoto's thyroiditis.

14. Other auto immune disease commonly associated with hashimoto's thyroiditis is segmental vitiligo & type 1 DM.

CONCLUSION

- Hashimoto's thyroiditis is a commonly present as diffuse euthyroid goitrous enlargement.
- Females are more prone to develop Hashimoto's thyroiditis. The proportion of younger age group females more commonly involved in our study group (north Chennai).
- Hashimoto's thyroiditis has a varied clinical presentation and as such couldPresent as a diffuse goiter, a multinodular goitre or a solitary nodule.Diffuse goiter is more common.
- Hashimoto's thyroiditis could present in a hypothyroid state, an euthyroid State, subclinical hypothyroidism, subclinical hyperthyroidism and in a small proportion of the patients in a hyperthyroid state.
- Diagnosis of Hashimoto's thyroiditis could be done by FNAC, positiveAntibody titres or final histopathology.
- Anti TPO levels correlates with severity of the disease.
- Treatment is primarily medical with thyroxine replacement or suppression.
- Surgery is rarely required.
- Diffuse goiters and solitary nodules respond better to the medical line of management, than do multinodular goiters.
-

PROFORMA

Name: I.P/O.PNo.

Age: Date of Examination:

Sex:

Address:

Occupation:

COMPLAINTS WITH DURATION:

1. Swelling - Present / Absent

   Duration –

   Noticed by - Patient / Relatives / Doctor.

   Pain in the swelling - Present / Absent

   Recent rapid growth - Present / Absent

2. Change of Voice - Present / Absent
3. Difficulty in Swallowing - Present / Absent
4. Difficulty in Breathing - Present / Absent
5. Hoarseness of Voice - Present / Absent
6. Symptoms of Toxicity -

   Palpitation –

   Weight Loss –

   Excessive Sweating –

   Increased Appetite –

   Heat intolerance –

7. Symptoms of Hypothyroidism -

Weigh gain –

Cold intolerance –

Constipation–

PAST HISTORY

History of any medical illness –

Prior drug history –

History of and prior surgery –

History of any neck irradiation –

FAMILY HISTORY

Unmarried / Married -

Any similar complaints in the family -

PERSONAL HISTORY

Diet –

Appetite –

Bowel and Bladder –

Sleep –

Habits –

PHYSICAL EXAMINATION

GENERAL EXAMINATION

Built - Ankle edema –

Nourishment - Anemia –

Temperature - Lymph node enlargement –

Clubbing - Cyanosis –

Pulse- B.P-

LOCAL EXAMINATION

Visible swelling - Present / Absent

Movement with deglutition Present / Absent

Movement with Protrusion of Tongue Present / Absent

Shape -

Size –

Location- Right lobe / Left lobe / Isthmus

Surface - Smooth / Irregular

Consistency - Soft / Cystic / Firm / Hard

Mobility - Present / Absent

Plane of Swelling -

Position of Trachea - Midline / Deviated

Carotid Pulsation - Normal / Deviated

Lymph Nodes - Present / Absent

Girth of the Neck -

Signs of Toxicity

Exophthalmos - Present / Absent

Eye Signs - Present / Absent

Tremors - Present / Absent

Excessive Perspiration - Present / Absent

Bruit - Present / Absent

Signs of Hypothyroidism - Present/ Absent

SYSTEMIC EXAMINATION

C.V.S.

C.N.S.

R.S.

INVESTIGATIONS

Routine investigations

Hormonal Assay

TSH

T3

T4

FNAC

Antithyroid Antibodies

Anti TPO Ab-

< 35 negative

35-50 equivocal

- 50 positive

Anti Tg antibodies

< 225 negative

225-325 – equivocal

>325- positive

Other Investigations:

DIAGNOSIS:

TREATMENT

Medical :

FOLLOW UP

Date	Pulse	Weight	Consistency	girth of Neck	Comments	TFT

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KEY TO MASTER CHART

1. HYPO- HYPOTHYROIDISM
2. HYPER- -HYPERTHYROIDISM
3. DUR- DURATION IN MONTHS
4. SUBCLINICAL HYPO- SUBCLINICAL HYPOTHYROIDISM
5. SUBCLINICAL HYPER- SUBCLINICAL HYPERTHROIDISM
6. BMI – BODY MASS INDEX
7. T1DM- TYPE 1 DIABETES MELITIS
8. FLP- FASTING LIPID PROFILE
9. ANA- ANTINUCLEAR ANTIBODY
10. ECG- ELECTROCARDIOGRAM
11. BOTH- BOTH POSITIVE
12. Neg- BOTH NEGATIVE
13. P.SMEAR- PERIPHERAL SMEAR
14. m.c/h.c- MICROCYTIC HYPOCHROMIC ANEMIA
15. n.c/n.c- NORMOCYTIC NORMOCHROMIC
16. T.CH, LDL ↑- TOTAL CHOLESTEROL & LDL INCREASED
17. ANA- ANTI NUCLEAR ANTIBODY

SL.	NAME	AGE	SEX	ADDRESS		REFERRAL	OTHER COMPLAINTS	goiter	DUR	THYRIOD STATUS	ANTIBODIES	BMI	other disease	FLP	ECG	ANA	Hb / PCV	P.SMEAR
1	RUKKU	18	F	THIRUVOTTIYUR		GOITER	nil	diffuse	2	HYPOTHYROID	BOTH	23	k/c/o T1DM	N	N	neg	8.2/26	m.c/h.c
2	JENCI	16	F	MULLAI NAGAR		GOITER	nil	diffuse	1.5	EUTHYROID	BOTH	24		N	N	neg	9.6/30	m.c/h.c
3	SULEKA	17	F	GANTHI NAGAR		GOITER	hair loss	diffuse	6	EUTHYROID	BOTH	18		N	N	neg	11.2/34	n.c/n.c
4	SATYA	19	F	THIRUVOTTIYUR		GOITER	fatigabilty	diffuse	3	EUTHYROID	TPO	17		N	N	1:40+	10.2/32	m.c/h.c
5	RAMYA	18	F	THILAKAR NAGAR		GOITER	nil	diffuse	4	SUBCLINCAL HYPO	BOTH	26	k/c/o T1DM	N	N	neg	12.4/36	
6	SELVI	15	F	VASANTHA NAGAR		GOITER	hair loss	diffuse	2.5	EUTHYROID	neg	20		N	N	neg	13/40	
7	RANI	19	F	VOC NAGAR		GOITER	mennorhagia	diffuse	2	EUTHYROID	BOTH	25		N	N	1:40+	7.6/26	m.c/h.c
8	MUTHU	17	M	NEW WASHERMANPET		GOITER	nil	diffuse	1	EUTHYROID	TPO	24		N	N	neg	10.6/32	n.c/n.c
9	MALA	22	F	TONDIARPET		GOITER	skin rashes, arthalgia	diffuse	3	SUBCLINCAL HYPO	BOTH	23	SLE	N	N	1: 160 +	11.2/34	n.c/n.c
10	VENI	24	F	KORUKKUPET		GOITER	mennorhagia	diffuse	4	EUTHYROID	neg	26		N	N	neg	8.6/26	m.c/h.c
11	FATHIMA	28	F	ROYAPURAM		GOITER	nil	diffuse	8	SUBCLINCAL HYPO	TPO	24	k/c/o T1DM	N	lvc	neg	13.2/38	
12	SHARMILLA	27	F	VYASARPADI		GOITER	nil	diffuse	4	SUBCLINICAL HYPER	BOTH	18		N	N	neg	11.2/38	n.c/n.c
13	HEMA	25	F	THIRUVOTTIYUR		GOITER	mennorhagia	diffuse	4	EUTHYROID	TPO	17		N	N	1:40+	7.6/24	m.c/h.c
14	LATHA	29	F	VOC NAGAR		GOITER	nil	diffuse	2	SUBCLINCAL HYPO	BOTH	24	vitiligo	N	N	1:40	8.2/28	m.c/h.c
15	MARY	22	F	WASHERMANPET		GOITER	mennorhagia	diffuse	3	EUTHYROID	BOTH	23		N	N	neg	10.6/32	m.c/h.c
16	NAYAKI	25	F	ENNORE		GOITER	nil	MNG	7	HYPERTHROID	BOTH	21		N	N	1:40+	9.6/32	m.c/h.c
17	CHANDRA	24	F	THIRUVOTTIYUR		GOITER	hair loss	diffuse	3	EUTHYROID	TPO	18.5		N	N	neg	12.6/38	
18	PRIYA	27	F	THILAKAR NAGAR		GOITER	infertility -2 yrs	diffuse	3	HYPOTHYROID	BOTH	20.5		T CH & LDL ↑	N	neg	11.4/36	n.c/n.c
19	VASANTHA	24	F	ROYAPURAM		GOITER	nil	diffuse	1	SUBCLINICAL HYPER	BOTH	28		N	lvc	neg	10.2/32	m.c/h.c
20	VANI	26	F	ENNORE		GOITER	hair loss	diffuse	2	EUTHYROID	TPO	25	vitiligo	N	N	1:40+	13/40	
21	KALA	27	F	WASHERMANPET		GOITER	nil	diffuse	1	EUTHYROID	BOTH	17.6		N	N	1:40+	9.8/32	m.c/h.c
22	JEYA	24	F	VOC NAGAR		GOITER	infertility -4yrs	diffuse	2	SUBCLINCAL HYPO	neg	20		N	N	neg	10.2/34	m.c/h.c
23	DEVI	26	F	VYASARPADI		GOITER	nil	diffuse	2	EUTHYROID	BOTH	22		N	N	1:40+	12.6/38	
24	DIYVA	26	F	NEW		GOITER	nil	MNG	5	EUTHYROID	TPO	21		N	N	neg	13/42	

				WASHERMANPET														
25	SAROJA	23	F	ENNORE		GOITER	myalgia	diffuse	3	SUBCLINCAL HYPO	BOTH	25		N	N	1:40+	9.8/30	m.c/h.c
26	GANESH	28	M	GANTHI NAGAR		GOITER	nil	diffuse	4	HYPERTHYROID	BOTH	26		N	N	neg	12.4/36	
27	MONISHA	29	F	KORUKKUPET		GOITER	nil	diffuse	4	EUTHYROID	TPO	22		N	N	neg	10.4/32	m.c/h.c
28	MEENA	28	F	ENNORE		GOITER	nil	diffuse	3	HYPOTHYROID	BOTH	27	vitiligo	T CH & LDL ↑	lvc	neg	10.4/32	m.c/h.c
29	BAVANI	25	F	THIRUVOTTIYUR		GOITER	nil	diffuse	5	EUTHYROID	TGb	22		N	N	1:40+	12.4/40	
30	STELLA	27	F	THILAKAR NAGAR		GOITER	nil	MNG	7	SUBCLINCAL HYPO	neg	21		N	N	neg	9.6/32	m.c/h.c
31	MUMTAJ	24	F	WASHERMANPET		GOITER	infertility -2 yrs	diffuse	1	EUTHYROID	BOTH	23.5		N	N	neg	12.6/40	
32	RATHI	26	F	NEW WASHERMANPET		GOITER	nil	diffuse	1	SUBCLINCAL HYPO	BOTH	26		T CH & LDL ↑	N	neg	10.2/32	m.c/h.c
33	GEETHA	30	F	ROYAPURAM		GOITER	infertility- 5 yrs	diffuse	1.5	SUBCLINCAL HYPO	BOTH	23.4		NN	N	neg	8.6/28	m.c/h.c
34	SHANTHI	33	F	VOC NAGAR		GOITER	nil	diffuse	2	SUBCLINICAL HYPER	BOTH	25		NN	N	neg	12.4/40	
35	BOMMI	35	F	MANALI		GOITER	nil	diffuse	7	EUTHYROID	BOTH	23		NN	N	neg	12.6/42	
36	UMA	37	F	TONDIARPET		GOITER	myalgia	diffuse	2	EUTHYROID	BOTH	25		N	N	neg	10.2/32	m.c/h.c
37	DURGA	39	F	KORUKKUPET		GOITER	nil	diffuse	2	HYPOTHYROID	BOTH	21	DISTAL RTA	T CH & LDL ↑	lvc	neg	9.6/32	m.c/h.c
38	BINDU	36	F	MANALI		GOITER	nil	diffuse	4	EUTHYROID	BOTH	20		N	N	neg	12.8/42	
39	THAYAR	37	F	THIRUVOTTIYUR		GOITER	nil	diffuse	1	SUBCLINCAL HYPO	BOTH	22		N	N	neg	10.4/32	m.c/h.c
40	BANU	36	F	KORUKKUPET		GOITER	nil	diffuse	1	SUBCLINICAL HYPER	BOTH	24		N	N	neg	12.4/40	
41	DESAM	32	F	ENNORE		GOITER	nil	MNG	5	EUTHYROID	BOTH	19		N	N	neg	13/42	
42	RANJANI	38	F	VOC NAGAR		GOITER	myalgia	diffuse	5	SUBCLINCAL HYPO	TGb	17		N	N	neg	10.2/32	m.c/h.c
43	PUSPHA	39	F	WASHERMANPET		GOITER	nil	diffuse	6	EUTHYROID	BOTH	22		N	N	neg	14/44	
44	GOKILA	34	F	MANALI		GOITER	nil	diffuse	4	HYPOTHYROID	TGb	23	vitiligo	T CH & LDL ↑		neg	10.4/32	m.c/h.c
45	MEGALA	30	F	ROYAPURAM		GOITER	nil	diffuse	4	SUBCLINICAL HYPER	BOTH	27		N	N	neg	12.6/44	
46	JAMUNA	37	F	TONDIARPET		GOITER	myalgia	diffuse	4	SUBCLINCAL HYPO	BOTH	26		N	N	neg	9.6/32	m.c/h.c
47	ANJALAI	37	F	VYASARPADI		GOITER	myalgia	diffuse	4	EUTHYROID	BOTH	28.6		N	N	neg	14/45	
48	VIJAYA	35	F	ROYAPURAM		GOITER	nil	SNG	3.5	EUTHYROID	BOTH	22		T CH & LDL ↑	N	neg	13/40	
49	ROSE	45	F	ENNORE		GOITER	myalgia	diffuse	3	subclinical hypo	TPO	21		N	N	neg	10.6/32	m.c/h.c

50	SELIN	43	F	VOC NAGAR		GOITER	nil	diffuse	5	HYPERTHYOID	BOTH	17		N	ST	1:40+	13/44	
51	AMEENA	48	F	WASHERMANPET		GOITER	myalgia	diffuse	5	SUBCLINICAL HYPER	TPO	19		N	N	neg	10.6/30	m.c/h.c
52	AMMU	44	F	MANALI		GOITER	nil	diffuse	4	EUTHYROID	TPO	25.8		N	N	1:40+	14/46	
53	MEENA	40	F	GANTHI NAGAR		GOITER	nil	diffuse	7	subclinical hyper	BOTH	26		N	N	neg	9.2/32	m.c/h.c
54	AMUL	47	F	MULLAI NAGAR		GOITER	myalgia	SNG	7	EUTHYROID	BOTH	22		N	N	neg	14/45	
55	KANAGA	42	F	VASANTHA NAGAR		GOITER	myalgia	diffuse	7	EUTHYROID	BOTH	24		T CH & LDL ↑	N	neg	12.4/42	
56	PRIYANKA	49	F	VYASARPADI		GOITER	nil	diffuse	5	SUBCLINCAL HYPER	BOTH	23		N	N	neg	10.4/32	m.c/h.c
57	PUSPHA	47	F	ROYAPURAM		GOITER	nil	diffuse	7	EUTHYROID	BOTH	18		N	N	neg	13/40	
58	JAYA	42	F	ENNORE		GOITER	myalgia	diffuse	4	EUTHYROID	BOTH	19		T CH & LDL ↑	N	neg	10.6/32	m.c/h.c
59	STEELA	52	F	WASHERMANPET		GOITER	nil	diffuse	4	EUTHYROID	BOTH	19.5		N	N	neg	13.8/46	
60	KAMATCHI	51	F	THIRUVOTTIYUR		GOITER	nil	diffuse	4	SUBCLINICAL HYPER	BOTH	20.6		N	N	neg	15/46	